BMJ open

The Incidence of Eating Disorders in the UK in 2000-2009: findings from the General Practice Research Database

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-002646
Article Type:	Research
Date Submitted by the Author:	28-Jan-2013
Complete List of Authors:	micali, nadia; UCL Institute of Child Health, Hagberg, Katrina; Boston Collaborative Drug Surveillance Program, Boston University School of Public Health, Petersen, Irene; University College London Medical School, Department of Primary Care and Population health Treasure, Janet; King's College London, Institute of Psychiatry, Eating Disorders Research Unit
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Mental health
Keywords:	Eating disorders < PSYCHIATRY, EPIDEMIOLOGY, PRIMARY CARE

SCHOLARONE™
Manuscripts

For peer review only

The Incidence of Eating Disorders in the UK in 2000-2009: findings from the General Practice Research Database

Nadia Micali, MD, PhD, MRCPysch

Behavioural and Brain Sciences Unit, Institute of Child Health, University College London, 30 Guilford Street, WC1N 1EH, UK

Katrina W Hagberg, MPH

Boston Collaborative Drug Surveillance Program, Boston University School of Public Health, Lexington MA 02421 US

Irene Petersen, PhD

Department of Primary Care and Population health, University College London Medical School, Rowland Hill Street London, NW3 2PF

Janet L Treasure , MD, PhD, FRCP, FRCPsych

Eating Disorders Research Unit, Dept. of Psychological Medicine, King's College London, Institute of Psychiatry, London, SE5 8AZ UK

For peer review only

Keywords: epidemiology, incidence, eating disorders, primary care

Word count: 3,056

ABSTRACT

Objectives: Few studies have investigated the incidence of eating disorders (ED). Important questions about changes in incidence of diagnosed disorders in recent years, disorder and gender-specific onset and case detection remain unanswered. Understanding changes in incidence is important for public health, clinical practice and service provision. The aim of this study was to estimate annual (age-, gender-, and subtype-specific) incidence of diagnosed ED: anorexia nervosa, bulimia nervosa and eating disorder not otherwise specified (EDNOS) in primary care over a ten-year period in the UK (2000-2009); to examine changes within the study period; and to describe peak age at diagnosis.

Design: Register-based study.

Setting: Primary care. Data were obtained from a primary care register, the General Practice Research Database, which contains anonymised records representing about 5% of the UK population.

Participants: All patients with a first time diagnosis of anorexia nervosa, bulimia nervosa and EDNOS were identified.

Primary outcome: Annual crude and age-standardized incidence rates were calculated.

Results: A total of 9,062 patients with a first time diagnosis of an ED were identified. The age-standardized annual incidence rate of all diagnosed ED for ages 10-49 increased from 32.3 (95% confidence interval (CI): 31.7-32.9) to 37.2 (95%CI: 36.6-37.9) per 100,000 between 2000 and 2009. The incidence of anorexia and bulimia nervosa was stable; however the incidence of EDNOS increased. The incidence of diagnosed ED was highest for females aged 15-19 and for males aged 10-14.

Conclusions: The age-standardized incidence of ED increased in primary care between 2000 and 2009. New diagnoses of EDNOS increased and EDNOS is the most common eating disorder in primary care.

For peer review only

ARTICLE SUMMARY:

Article focus:

-Determining incidence rates of eating disorders in primary care in the United Kingdom between 2000 and 2009 by age group and gender.

-Investigating changes in incidence of eating disorders between 2009 and 2000.

-Identify age peaks at incidence by gender

Key messages:

-The incidence of eating disorders varied by gender and eating disorder-type. Eating disorder not otherwise specified was the most common incident eating disorder in males and females

- There was a significant increase during the ten years under study in the overall incidence of diagnosed eating disorders both in males and females

-Peak age at diagnosis varied across genders and by eating disorder-type. Adolescent girls aged 15-19 had the highest incidence of eating disorders (2 per 1000).

Strengths and limitations of this study:

-This study is representative of the UK population

-Incidence rates obtained from primary care allow inclusion of all cases presenting to healthcare settings, not just cases presenting to secondary/tertiary care (referral bias)

-However incidence rates obtained in this study are likely to be an underestimate of incident caes present in the community

For peer review only

INTRODUCTION

Eating Disorders (ED) are severe chronic mental health disorders, associated with negative outcomes and the highest mortality amongst psychiatric disorders.[1][2] Understanding changes in their incidence over time and variations by gender and age is important in aiding causal investigations and service provision. Differences across studies in the incidence of EDs have been reported, mainly due to the different populations and nature of the samples studied: primary care registers [3, 4] or community samples.[5, 6] Due to the relatively low incidence rates of ED in the community, studying the incidence of ED at community level is extremely difficult and costly, hence electronic databases and primary care registers can play an important role in understanding changes in the number of individuals developing a disorder and seeking help.

Most studies so far have highlighted consistent incidence rates in primary care (i.e. a stable number of individuals with a new ED diagnosis) for anorexia nervosa (AN) in the 1980s and 1990s, however a recent Dutch study highlighted an increase in the incidence of AN in females aged 15-19 in the 1990s compared to the 1980s.[4] With regards to bulimia nervosa (BN), after an increase in new diagnoses in the 1980s and mid 1990s [3, 7, 8] recent findings have suggested a possible decrease or stabilization since the late 1990s. [3, 4]

Unspecified Eating Disorders, commonly grouped under the “not Otherwise Specified” diagnostic category (EDNOS) have been far less studied than AN and BN. Although EDNOS is the disorder most commonly seen in secondary/tertiary care settings [9, 10] and in general population samples [11] the incidence of EDNOS has not been previously estimated in primary care.

We aimed to: 1. estimate the incidence rates of ED, as well as incidence rates of AN, BN and EDNOS separately, in primary care in the United Kingdom between 2000 and 2009 by age group and gender; 2.

For peer review only

investigate whether the incidence of diagnosed ED changed in 2009 compared to 2000; 3. identify peaks in the incidence of diagnosed ED by gender and age group.

Method:

Sample

We used data from the General Practice Research Database (GPRD), a large automated anonymised UK medical record database containing information from some 400 general practices with cumulative follow-up time of more than 40 million person-years (representing approximately 5% of the general UK population). The comprehensive nature of the information on clinical diagnoses and drug exposure recorded in the GPRD has been repeatedly validated and found to be of high quality for the purpose of conducting epidemiological research.[12, 13] The general practitioners (GPs) who contribute data to the GPRD use office computers in their routine practice to record medical information including demographic data, medical diagnoses, and deaths in a standard, anonymous format and agree to provide data for research purposes to the GPRD. The practices included are broadly representative of UK general practices in terms of geographic distribution, gender and age of registered patients, and practice size.[14]

Validity of diagnoses

The comprehensive nature of the information on clinical diagnoses recorded in the GPRD has been repeatedly validated and found to be of high quality for the purpose of conducting epidemiological research [12, 13] (for a systematic review see [16, 17]). In particular ED diagnoses were found to have a positive predictive value of >90% [8, 17], therefore reliable for identifying ED cases.

The period for this study was 1 January 2000 through 31 December 2009.

For peer review only

We identified all subjects aged 10-49 years for whom data were recorded in the GPRD during the study period.

Case Definition

Patients were identified as incident cases of ED if they had a first time diagnosis of AN, BN or EDNOS recorded in their computerized medical record between 1st January 2000 and 31st December 2009 with no prior recorded ED diagnosis. We used diagnostic codes from a modified version of the Read classification system (specific codes available on request).[15] To be eligible for inclusion, patients had to have been registered with the GP for at least 6 months before the first recorded diagnosis and to be 10 to 49 years of age at the time of diagnosis. This age-range was chosen given the very rare number of new onset cases before age 10 and after age 49.[3, 8] Information on weight and height and Body Mass index (BMI) at the time of diagnosis was also evaluated by one of the authors (NM) for 10% of all records (where this information was available in the computerized record).

Cases were classified according to the type of ED (AN, BN, or EDNOS) that was recorded.
All cases receiving a diagnosis of EDNOS were identified using the "ED unspecified" code (extracted codes are based on the International Classification of Diseases and Related Health Problems, *tenth revision* - ICD-10,[16] which uses the "Eating Disorder unspecified" notation for EDNOS). EDNOS cases did not have a prior or subsequent diagnosis of either AN or BN within the study period.
Records of patients who received more than one diagnosis of AN and BN within 3 months were all reviewed by hand and BMI and ED symptoms recorded at the time of diagnosis were used to classify the patient's ED type. In instances where a patient had a diagnosis of both AN and BN within 3 months and the subject had a BMI and symptoms consistent with one diagnosis only (AN or BN) at the time of diagnosis they were considered an incident case of either AN or BN. If neither BMI nor symptoms were

For peer review only

recorded at the time of diagnosis and the two diagnoses were recorded at least one month apart or if BMI or symptoms were consistent with having both AN and BN then the patient was classified as having an incident case of both AN and BN. If the patient received AN and BN diagnoses on the same day and no BMI or symptoms were recorded we assumed the patient had an ED but could not assign them to AN or BN, therefore they were classified as having EDNOS.

The index date was the date of the first diagnosis of AN, BN, or EDNOS recorded by the GP.

Incidence rates

Total, age-, gender- and year- specific annual incidence rates (IR) of ED diagnoses (all types) and 95% confidence intervals (CI) were calculated. The number of incident cases were divided by the number of subjects aged 10 to 49 registered in GPRD during the calendar year under study (the population at risk). We stratified the annual IRs by age group (10-14, 15-19, 20-29, 30-39 and 40-49 years), gender, and type of ED recorded (AN, BN, or EDNOS).

Age-standardized annual IR for eating disorders were calculated using the direct method, using annual mid-year UK population estimates for the UK data for 2000 and 2009 obtained from the Office of National Statistics (ONS) [14] and 95% confidence intervals were calculated based on the Poisson approximation. Standardised rates were calculated for all and by gender and used to compare changes in recorded incidence between 2000 and 2009 using the *iri* command in Stata 12 (Stata Corp.).

We calculated stratified age and gender specific IR by ED diagnosis for the year 2009.

Ethics

For peer review only

The protocol for this study was reviewed and approved by the Independent Scientific Advisory Committee (ISAC) of the Medicines and Healthcare Products Regulation Agency (MHRA).

Results

We identified 9,062 patients with a first time diagnosis of ED (AN, BN, or EDNOS) recorded in the GPRD during the study period (2000-2009).

Cases with co-occurring diagnoses were reviewed by hand. Among the 73 patients who received a first time diagnosis of AN and BN within a 3 month period, 18 cases were classified as incident cases of AN; 23 were classified as incident cases of BN. In 25 cases both AN and BN diagnoses were plausible and these were considered to have both an incident AN and BN diagnosis. Seven cases received two diagnoses on the same day and these cases were considered to have incident EDNOS.

A total of 2,134 cases (23.5%) were classified as incident cases of AN during the study period; 3,433 cases (37.8%) were considered incident cases of BN; and 3,505 (38.6%) were classified as incident cases of EDNOS.

Annual Incidence Rates

Annual Crude IR of all ED across genders and stratified by gender are shown in the supplemental table (Table S1). The overall crude IR of diagnosed ED was 33.0 (95%CI: 30.7-35.3) in 2000 and 36.8 (95%CI: 34.4-39.2) per 100,000 in 2009. (See table 1).

Age-standardized rates of ED were: 32.3 (95%CI: 31.7-32.9) per 100,000 in 2000 and 37.2 (95%CI: 36.6-37.9) per 100,000 in 2009; showing a statistically significant increase ($p<0.000001$) (see table 1).

For peer review only

Gender-specific Incidence Rates

Females

There was evidence that the incidence of all ED steadily increased in the period under study for females aged 10-49 (see Figure 1). The incidence of diagnosed ED in last 3 years of the study period (2007-2009) was higher compared to 2000-2002 with a peak of 63.8 (59.7-68.2) per 100,000 in 2008 (see table S1).

The age-standardised rates of ED in females significantly increased between 2000 and 2009 from 51.8 (95%CI: 50.6-52.9) per 100,000 to 62.6 (95%CI: 61.4-63.8) in 2009 (p<0.00001) (see Table 1).

The incidence of AN in females was stable during the study period despite some minor fluctuations across the years (Figure 1). A formal comparison between the annual IR of diagnosed AN in 2000 and 2009 showed no differences in rates.

The incidence of BN also remained stable during the first decade of the 2000s (see Figure 1).

There was evidence of a steady increase in the incidence of diagnosed EDNOS in females aged 10-49 during the study period. In 2000 the IR was 17.4 (95%CI: 15.3-20.0) per 100,000 compared to 27.6 (95%CI: 24.9-30.6) per 100,000 in 2009 (see Table S1 and Figure 1). There was a significant increase in 2009 compared to 2000 (p<0.00001). During the time under study EDNOS became the most common incident ED diagnosis in females aged 10-49 (figure 1).

Males

The annual crude and age-standardized incidence estimates were similar and increased during the study period (see Table 1). The annual age-standardized incidence of diagnosed ED in males significantly

For peer review only

increased from 5.6 (95%CI: 5.3-6.0) per 100,000 in 2000 to 7.1 (95%CI: 6.7-7.5) per 100,000 in 2009 ($p<0.00001$).

The incidence of diagnosed AN in males remained stable during the study period (see figure 2). The difference in IR between 2000 and 2009 was not statistically significant.

The incidence of BN in males also remained stable between 2000 and 2009 (see figure 2).

EDNOS was the most common diagnosis in males during the study period with an incidence of 3.3 (95%CI: 2.3-4.5) per 100,000 in 2000 and 4.1 (95%CI: 3.1-5.3) per 100,000 in 2009 (see Table S1), representing a 24% increase from 2000 to 2009.

Age-specific Incidence Rates in 2009

Females

In 2009 the crude IR for diagnosed ED for females aged 10-49 was 62.7 (95%CI: 58.4-67.1) per 100,000 (see Table 1).

The highest incidence of AN, BN and EDNOS was for females between 15 and 19 years of age (see Table 3). In this age range the IR for all diagnosed ED was 164.5 (95%CI: 144.6-186.4) per 100,000 (0.2%) (Table 2). Although the peak age at incident diagnosis for both AN and for BN was 15-19 years, 24.0 (95%CI: 16.3-34.3) per 100,000 girls had an onset of AN between the ages of 10-14 years. In contrast, diagnoses of BN peaked between 15-19 years and IR continued to be elevated for those aged 20-29 years (see table 3).

EDNOS was the most common incident diagnosed ED among females aged 10-49: 27.6 (95% CI: 24.9-30.6) per 100,000 in 2009.

For peer review only

Males

In 2009 the crude IR for diagnosed ED for males aged 10-49 years was 7.1 (95%CI: 5.7-8.8) per 100,000 (see Table S1). The peak age of incidence of diagnosed AN in males was 15-19 years (IR=3.8 per 100,000, 95%CI: 1.4-8.3). Diagnosed BN peaked between ages 20 and 29: 4.7 (95%CI: 2.6-7.8) per 100,000. In contrast to females, EDNOS diagnoses in boys peaked between 10-14 years of age (IR= 15.0 per 100,000, 95%CI: 9.1-23.2). EDNOS was the most common diagnosed ED in males aged 10-49 (IR=4.1 per 100,000, 95%CI: 3.1-5.4) (See Table S1).

In 2009 the female to male ratio for AN was 10.2:1, for BN 12.9:1; and 6.7:1 for EDNOS.

Discussion

This is the most comprehensive study of the incidence of eating disorders in primary care to date including ~ 40 million person-years of follow-up. We showed that the annual age-standardized incidence of ED in the UK significantly increased between 2000 and 2009. This increase was due to a higher number of new EDNOS diagnoses in the last third of the decade, whilst the number of new diagnoses of AN and BN remained stable across the study period. The peak age of onset for an ED diagnosis in females was between 15 and 19 years. In this age range the incidence of ED for females was 0.2% of the population in 2009. A slightly different pattern of incident diagnosis was observed for males, with the peak age of onset at 15-19 years for AN, 10-14 years for EDNOS, and 20-29 years of age for BN.

This is the first study to investigate the incidence of all ED, including EDNOS, in primary care. Incidence rates of diagnosed AN in the current study were consistent with previous studies on the incidence of AN in the UK using the GPRD. [3, 8] A study using a primary care sample in the Netherlands highlighted an increased incidence rate of AN among adolescent girls in the 1990s;[4] whilst 15-19 was the peak age at

For peer review only

diagnosis of AN in our study, we found an incidence rate for girls in this age group of 49.6 per 100,000 in 2009; lower than the 109.2 per 100,000 person years reported in the Dutch Study during the 1990s.[4]

Despite some indications of a decreasing incidence of BN in the late 1990s, [3, 4] in the 2000s our study suggests a stabilization of incidence since the late 1990s. As suggested by Currin et al. [3] peaks of newly diagnosed cases in the mid and late 1990s probably corresponded to increased recognition and detection of a relatively "new" disorder, which has now stabilized at its true level.

This is to our knowledge the first study to estimate the incidence of EDNOS in primary care. Although this disorder was previously considered as encompassing a group of patients with less severe disorders than the classical AN and BN, recent focus on the impact and epidemiology of EDNOS [10, 19, 20] has highlighted its clinical and public health impact. EDNOS is not only acknowledged as the most prevalent ED in clinical and epidemiological samples [9, 10, 21] but it also is as severe as AN and BN in terms of clinical impact and outcomes.

Our findings of an increase in ED diagnoses over the first decade of the 2000s is consistent with two not-mutually exclusive possible explanations: the increase might be secondary to improved recognition and diagnosis at a primary care level, or a true increase in the number of subjects developing ED.

This possibly explains the highlighted increase in EDNOS diagnoses in the later part of the 2000s, maybe secondary to the increased research carried out on EDNOS resulting in increased awareness to the wider spectrum of ED that do not fit into diagnoses of AN and BN. However increased diagnoses might also result from increased presentations to primary care, due to a true increase in disorders.

For peer review only

Strengths and limitations

The GPRD is one of the largest sources of primary care data in the world. Using such a large and independently collected dataset, largely representative of GP practices in the UK, allowed us to estimate the incidence of presentations in a general practice setting. Access to primary care is universal in the UK, therefore results of this study are generalizable to the UK population. Moreover estimating incidence rates in a primary care setting ensures inclusion of mild cases, who normally would not be referred on to specialist services. Given the nature of GPRD we were unable to systematically ensure all diagnoses met DSM-IV or ICD-10 criteria for ED, however general practitioners incorporate data from secondary or tertiary care in the GPRD electronic records when patients are referred, therefore it is possible that some diagnoses included in the database were in fact made by psychiatrists. Moreover, GP diagnoses of eating disorders (and of mental health disorders) in GPRD have been shown to be highly valid.[18, 19] If patients were misclassified it is likely that the diagnostic subgroup might change but not the total incidence of ED diagnoses.

Given that our incidence rates are derived from primary care diagnoses, they allow ascertainment of "detected" incidence rates rather than community incidence rates (see figure 3) and are a close reflection of healthcare need. There is evidence that true rates might be double or triple those detected in a healthcare setting. [5, 6]

Conclusions

In summary, the incidence of diagnosed ED in the UK significantly increased between 2009 and 2000. The incidence of AN and BN has remained stable in males and females in the first decade of the 21st century; however the incidence of EDNOS increased.

At the peak age of diagnosis (age 15-19 years), it is estimated that 2 girls per 1000 are likely to be newly diagnosed with an ED in the UK. The incidence in this age group suggests that ED may be the most

For peer review only

common new onset mental health disorder in adolescent girls after depression [22]. In females aged 10-19 the incidence rate of ED is about 9-fold higher than the incidence rate of diagnosed type 1 diabetes in the UK (1.2 per 1,000 for ED vs. 0.26 per 1,000 for type 1 diabetes), and about half that of Type-2 diabetes (3.6 per 1,000).[23]

Future research should clarify whether the increase seen in this study reflects a true community increase or better detection. Our findings have important implications for public health, healthcare provision and understanding the development of eating disorders.

Funding:

This research was funded by a National Institute of Health Research (NIHR) clinician scientist award to Dr N Micali. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

The authors declare that they have no conflict of interest.

Author contributions:

Conception and design: Micali, Treasure

Analysis and interpretation of data and drafting the article: Micali, Hagberg, Treasure, Petersen

Critical revision of the manuscript: Treasure, Hagberg, Petersen

Data Sharing:

No unpublished data available.

Competing Interests:

None

For peer review only

References

1. Arcelus J, Mitchell AJ, Wales, J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders: a Meta analysis of 36 studies. *Arch Gen Psychiatry* 2011;68(7):724-731.
2. Field AE, Sonnenville K, Micali N, et al. Common eating disorders predictive of adverse outcomes are missed by the DSM-IV and DSM-5 classifications. *Pediatrics* 2012;130:e289-e295. doi: 10.1542/peds.2011-3663 Published online 16 July 2012.
3. Currin L, Schmidt U, Treasure J, Jick H. Time trends in eating disorder incidence. *Br J Psychiatry* 2005;186:132-135.
4. Van Son GE, van Hoeken D, Bartelds AI, et al. Time trends in the incidence of eating disorders: a primary care study in the Netherlands. *Int J Eat Disord* 2006;39(7):565-9.
5. Keski-Rahkonen A, Hoek HW, Susser ES, et al. Epidemiology and Course of Anorexia Nervosa in the Community. *Am J Psychiatry* 2007;164(8):1259-1265.
6. Keski-Rahkonen A, Hoek HW, Linna MS, et al. Incidence and outcomes of bulimia nervosa: a nationwide population based study. *Psychol Med* 2009;39(5):823-831.
7. Hoek HW, Bartelds AI, Bosveld JJ, et al. Impact of urbanization on detection rates of eating disorders. *Am J Psychiatry* 1995;152:1272-1278.
8. Turnbull S, Ward A, Treasure J, et al. The demand for eating disorder care. An epidemiological study using the general practice research database. *Br J Psychiatry* 1996;169:705-712.
9. Fairburn CG, Cooper Z, Bohn K, et al. The severity and status of eating disorder NOS: implications for DSM-V. *Behav Res Ther* 2007;45(8):1705-15.
10. Nicholls DE, Lynn R, Viner R. Childhood eating disorders: British national surveillance study. *Br J Psychiatry* 2011;198:295-301.

For peer review only

11. Wade TD, Bergin JL, Tiggemann M, et al. Prevalence and long-term course of lifetime eating disorders in an adult Australian twin cohort. *Aust N Z J Psychiatry* 2006;40(2):121-8.

12. Jick H, Terris BZ, Derby LE, Jick SS. Further validation of information recorded on a general practitioner based computerized data resource in the UK. *Pharmacoepidemiol Drug Saf*. 1992;1: 347-9.

13. Jick SS, Kaye JA, Vasilakis-Scaramozza C, et al. Validity of the general practice research database. *Pharmacotherapy* 2003;23:686-9.

14. Office for National Statistics. Key Health Statistics from general practice 1996: Series MB6 No1. London: Office for National Statistics; 1998.

15. Hammad TA, McAdams MA, Feight A, et al. Determining the predictive value of Read/OXMIS codes to identify incident acute myocardial infaraction in the General Practice Research Database. *Pharmacoepidemiol Drug Saf* 2008;17(12):1197-1201.

16. World Health Organisation . ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. World Health Organisation: Geneva. 1992

17. Herrett E, Thomas SL, Schoonen WM, et al. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol* 2010;69(1):4–14.

18. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60(572):e128-36.

19. Fairburn CG, Bohn K. Eating disorder NOS (EDNOS): an example of the troublesome "not otherwise specified" (NOS) category in DSM-IV. *Beh Res Ther* 2005;43(6):691-701.

20. Hay PJ, Mond J, Buttner P, Darby A. Eating Disorder Behaviors Are Increasing: Findings from Two Sequential Community Surveys in South Australia. *PLoS One* 2008;3(2): e1541.

For peer review only

21. Swanson SA, Crow SJ, Le Grange D, et al. Prevalence and correlates of eating disorders in adolescents. Results from the national comorbidity survey replication and adolescent supplement. *Arch Gen Psychiatry* 2011;68(7):714-23.

22. Wijlaars LP, Nazareth I, Petersen I. Trends in Depression and Antidepressant Prescribing in Children and Adolescents: A Cohort Study in The Health Improvement Network (THIN). *PLoS One* 2012;7(3):e33181.

23. González EL, Johansson S, Wallander MA, Rodríguez LA. Trends in the prevalence and incidence of diabetes in the UK: 1996-2005. *J Epidemiol Community Health* 2009;63(4): 332-6.

For peer review only

18

Table 1: Crude and age-standardized Incidence rates for eating disorders in 2000 and 2009 per 100,000 population

	2000			2009		
	No.	**Crude Incidence (95%CI)**	**Age-standardised Incidence (95%CI)**	**No.**	**Crude Incidence (95%CI)**	**Age-standardised Incidence (95%CI)**
Overall	789	33.0 (30.7-35.3)	32.3 (31.7-32.9)	897	36.8 (34.4-39.2)	37.2 (36.6-37.9)
Females	732	53.2 (49.5-57.2)	51.8 (50.6-52.9)	816	62.7 (58.4-67.1)	62.6 (61.4-63.8)
Males	57	5.6 (4.3-7.2)	5.6 (5.3-6.0)	81	7.1 (5.7-8.8)	7.1 (6.7-7.5)

For peer review only

19

Table 2: Incidence of ED per 100,000 population for the year 2009 by age and gender

ALL EATING DISORDERS						
Age (years)	Females			Males		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	74	116,476	63.5(50.2-79.3)	21	120,219	17.5 (11.1-26.2)
15-19	239	145,279	164.5 (144.6-186.4)	23	132,375	17.4 (11.3-25.6)
20-29	309	349,163	88.5 (79.4-98.8)	28	277,454	10.1 (6.8-14.4)
30-39	138	338,255	40.8 (34.4-48.0)	6	288,468	2.1 (0.8-4.3)
40-49	56	352,843	15.9 (12.1-20.5)	3	319,724	0.9 (0.2-2.5)

For peer review only

20

Table 3: Incidence of eating disorders per 100,000 population for the year 2009 by age, sex and type of eating disorder

ANOREXIA NERVOSA									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	28	116,476	24.0 (16.3-34.3)	3	120,219	2.5 (0.6-6.8)	31	236,695	13,1 (9.0-18.4)
15-19	72	145,279	49.6 (39.1-62.0)	5	132,375	3.8 (1.4-8.3)	77	277,654	27.7 (22.0-34.5)
20-29	69	349,163	19.8 (15.5-24.9)	6	277,454	2.2 (0.9-4.5)	75	626,617	12.0 (9.4-14.9)
30-39	12	338,255	3.5 (1.9-6.0)	1	288,468	0.3 (0.2-1.7)	13	626,723	2.1 (1.1-3.5)
40-49	5	352,843	1.4 (0.5-3.1)	1	319,724	0.3 (0.1-1.5)	6	672,567	0.9 (0.4-1.8)
10-49	**186**	**1,302,016**	**14.3 (12.3-16.4)**	**16**	**1,138,240**	**1.4 (0.8-2.2)**	**202**	**2,440,256**	**8.3 (7.1-9.5)**
BULIMIA NERVOSA									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence(95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	7	116,476	6.0 (2.6-11.9)	0	120,219	0	7	236,695	2.9 (1.1-5.6)
15-19	68	145,279	46.8 (36.6-58.9)	4	132,375	3.0 (0.9-7.3)	72	277,654	25.9 (20.1-32.4)
20-29	111	349,163	31.8 (26.3-38.1)	13	277,454	4.7 (2.6-7.8)	124	626,617	19.8 (16.4-23.2)
30-39	66	338,255	19.5 (15.2-24.7)	1	288,468	0.3 (0.2-1.7)	67	626,723	10.7 (8.3-13.4)
40-49	18	352,843	5.1 (3.1-7.9)	0	319,724	0	18	672,567	2.7 (1.6-3.8)
10-49	**270**	**1,302,016**	**20.7 (18.4-23.3)**	**18**	**1,138,240**	**1.6 (1.0-2.4)**	**288**	**2,440,256**	**11.8 (10.5-13.2)**
EATING DISORDER NOS (EDNOS)									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	39	116,476	33.5 (24.1-45.3%)	18	120,219	15.0 (9.1-23.2)	57	236,695	24.1 (18.4-31.0)
15-19	99	145,279	68.1 (55.7-82.6)	14	132,375	10.6 (6.0-17.3)	113	277,654	40.7 (33.7-48.7)
20-29	129	349,163	36.9 (30.9-43.4)	9	277,454	3.2 (1.6-5.9)	138	626,617	22.0 (18.6-25.9)
30-39	60	338,255	17.7 (13.6-22.7)	4	288,468	1.4 (0.4-3.3)	64	626,723	10.2 (7.9-13.0)
40-49	33	352,843	9.3 (6.5-13.0)	2	319,724	0.6 (0.1-2.0)	35	672,567	5.2 (3.7-7.1)
10-49	**360**	**1,302,016**	**27.6 (24.9-30.6)**	**47**	**1,138,240**	**4.1 (3.1-5.4)**	**407**	**2,440,256**	**16.7 (15.1-18.4)**

For peer review only

Supplemental Table 1: Annual incidence of eating disorders by gender and eating disorder type per 100,000 population

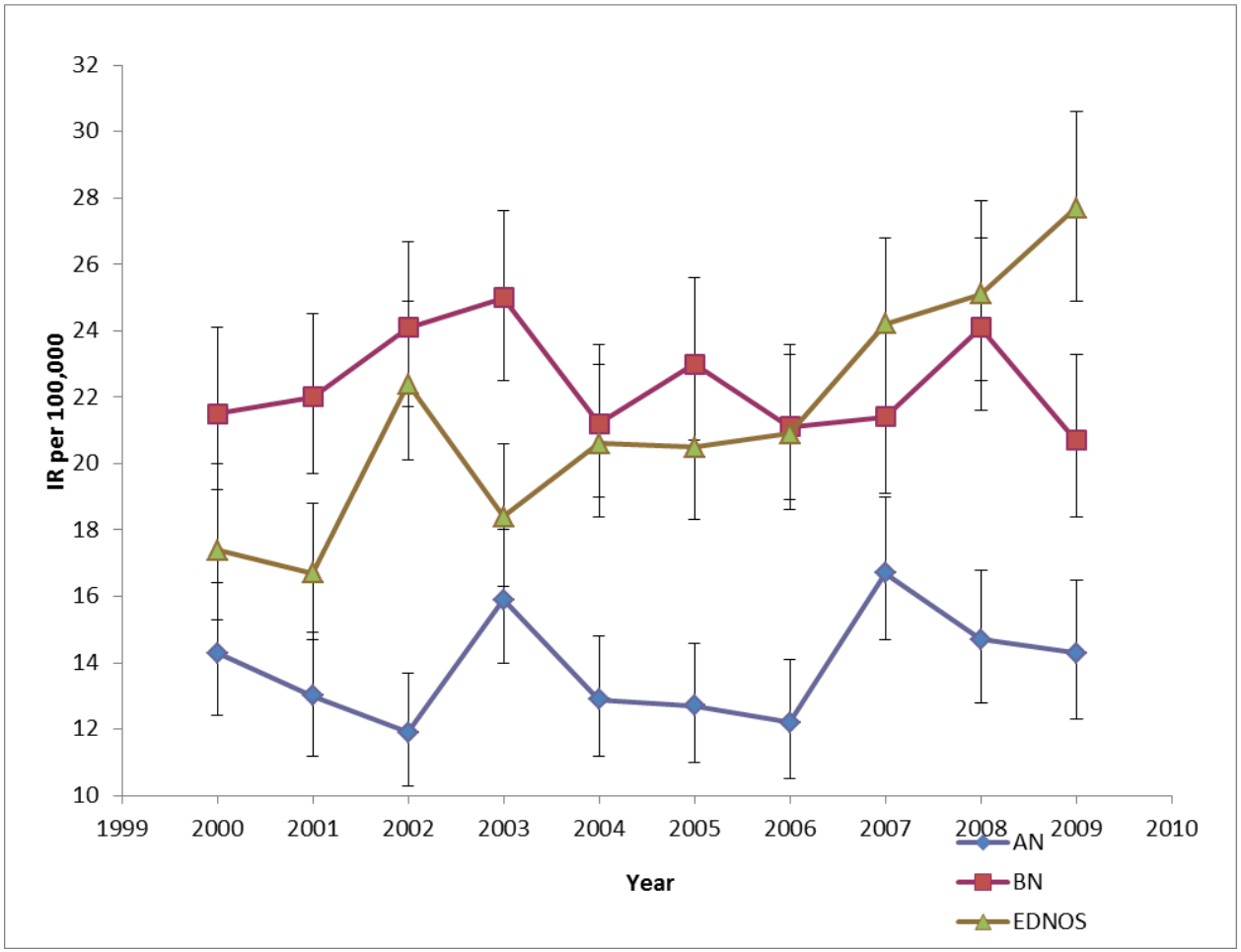
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
All Eating Disorders	789/2,393,179	838/2,673,109	953/2,703,550	967/2,740,803	904/2,827,344	906/2,819,275	882/2,786,786	980/2,680,119	946/2,553,593	897/2,440,256
Incidence (95% CI)	33.0 (30.7-35.3)	31.4 (29.3-33.5)	35.3 (33.1-37.5)	35.3 (33.1-37.6)	32.0 (29.9-34.1)	32.1 (30.0-34.3)	31.7 (29.6-33.8)	36.6 (34.3-38.9)	37.1 (34.7-39.5)	36.8 (34.4-39.2)
Males										
All ED	57/1,018,279	61/1,168,428	69/1,190,475	68/1,222,157	65/1,294,958	53/1,304,050	77/1,299,849	86/1,245,527	73/1,186,235	81/1,138,240
Incidence (95% CI)	5.6 (4.3-7.2)	5.2 (4.0-6.6)	5.8 (4.5-7.3)	5.6 (4.3-7.0)	5.0 (3.9-6.3)	4.1 (3.1-5.3)	5.9 (4.7-7.4)	6.9 (5.6-8.5)	6.1 (4.9-7.7)	7.1 (5.7-8.8)
AN	9/1,018,279	13/1,168,428	21/1,190,475	18/1,222,157	4/1,294,958	7/1,304,050	4/1,299,849	18/1,245,527	12/1,186,235	16/1,138,240
Incidence (95% CI)	0.9 (0.4-1.5)	1.1(0.6-1.8)	1.8 (1.1-2.7)	1.5 (0.9-2.3)	0.3 (0.1-0.7)	0.5 (0.3-0.9)	0.3 (0.1-0.7)	1.4 (0.8-2.2)	1.0 (0.5-1.7)	1.4 (0.8-2.2)
BN	14/1,018,279	14/1,168,428	14/1,190,475	13/1,222,157	20/1,294,958	15/1,304,050	20/1,299,849	18/1,245,527	22/1,186,235	18/1,138,240
Incidence (95% CI)	1.4 (0.8-2.3)	1.2 (0.7-2.0)	1.2 (0.7-1.9)	1.1 (0.6-1.8)	1.5 (1.0-2.3)	1.2 (0.7-1.9)	1.5 (1.0-2.3)	1.4 (0.9-2.2)	1.9 (1.2-2.8)	1.6 (1.0-2.5)
EDNOS	34/1,018,279	44/1,168,428	34/1,190,475	37/1,222,157	41/1,294,958	31/1,304,050	53/1,299,849	50/1,245,527	39/1,186,235	47/1,138,240
Incidence (95% CI)	3.3 (2.3-4.5)	3.8 (2.8-4.9)	2.9 (2.0-3.9)	3.0 (2.1-4.1)	3.2 (2.3-4.3)	2.4 (1.6-3.3)	4.1 (3.1-5.2)	4.0 (3.0-5.2)	3.3 (2.4-4.4)	4.1 (3.1-5.3)
Females										
All ED	732/1,374,900	777/1,504,681	884/1,513,075	899/1,518,646	839/1,532,386	853/1,515,225	805/1,486,937	894/1,434,592	873/1,367,358	816/1,302,016
Incidence (95% CI)	53.2 (49.5-57.2)	51.6 (48.0-55.4)	58.4 (54.6-62.4)	59.2 (55.4-63.2)	54.8 (51.1-58.5)	56.3 (52.6-60.2)	54.1 (50.5-58.0)	62.3 (58.3-66.5)	63.8 (59.7-68.2)	62.7 (58.4-67.1)
AN	197/1,374,900	195/1,504,681	180/1,513,075	241/1,518,646	198/1,532,386	193/1,515,225	181/1,486,937	240/1,434,592	201/1,367,358	186/1,302,016
Incidence (95% CI)	14.3 (12.4-16.4)	13.0 (11.2-14.9)	11.9 (10.3-13.7)	15.9 (14.0-18.0)	12.9 (11.2-14.8)	12.7 (11.0-14.6)	12.2 (10.5-14.1)	16.7 (14.7-19.0)	14.7 (12.8-16.8)	14.3 (12.3-16.5)
BN	296/1,374,900	331/1,504,681	365/1,513,075	379/1,518,646	325/1,532,386	349/1,515,225	314/1,486,937	307/1,434,592	329/1,367,358	270/1,302,016
Incidence (95% CI)	21.5 (19.2-24.1)	22.0 (19.7-24.5)	24.1 (21.7-26.7)	25.0 (22.5-27.6)	21.2 (19.0-23.6)	23.0 (20.7-25.6)	21.1 (18.9-23.6)	21.4 (19.1-23.9)	24.1 (21.6-26.8)	20.7 (18.4-23.3)
EDNOS	239/1,374,900	251/1,504,681	339/1,513,075	279/1,518,646	316/1,532,386	311/1,515,225	310/1,486,937	347/1,434,592	343/1,367,358	360/1,302,016
Incidence (95% CI)	17.4 (15.3-20.0)	16.7 (14.7-18.8)	22.4 (20.1-24.9)	18.4 (16.3-20.6)	20.6 (18.4-23.0)	20.5 (18.3-22.9)	20.9 (18.6-23.3)	24.2 (21.7-26.8)	25.1 (22.5-27.9)	27.7 (24.9-30.6)

ED: eating disorder; AN: anorexia nervosa, BN: bulimia nervosa, EDNOS: eating disorder not otherwise specified

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure 1

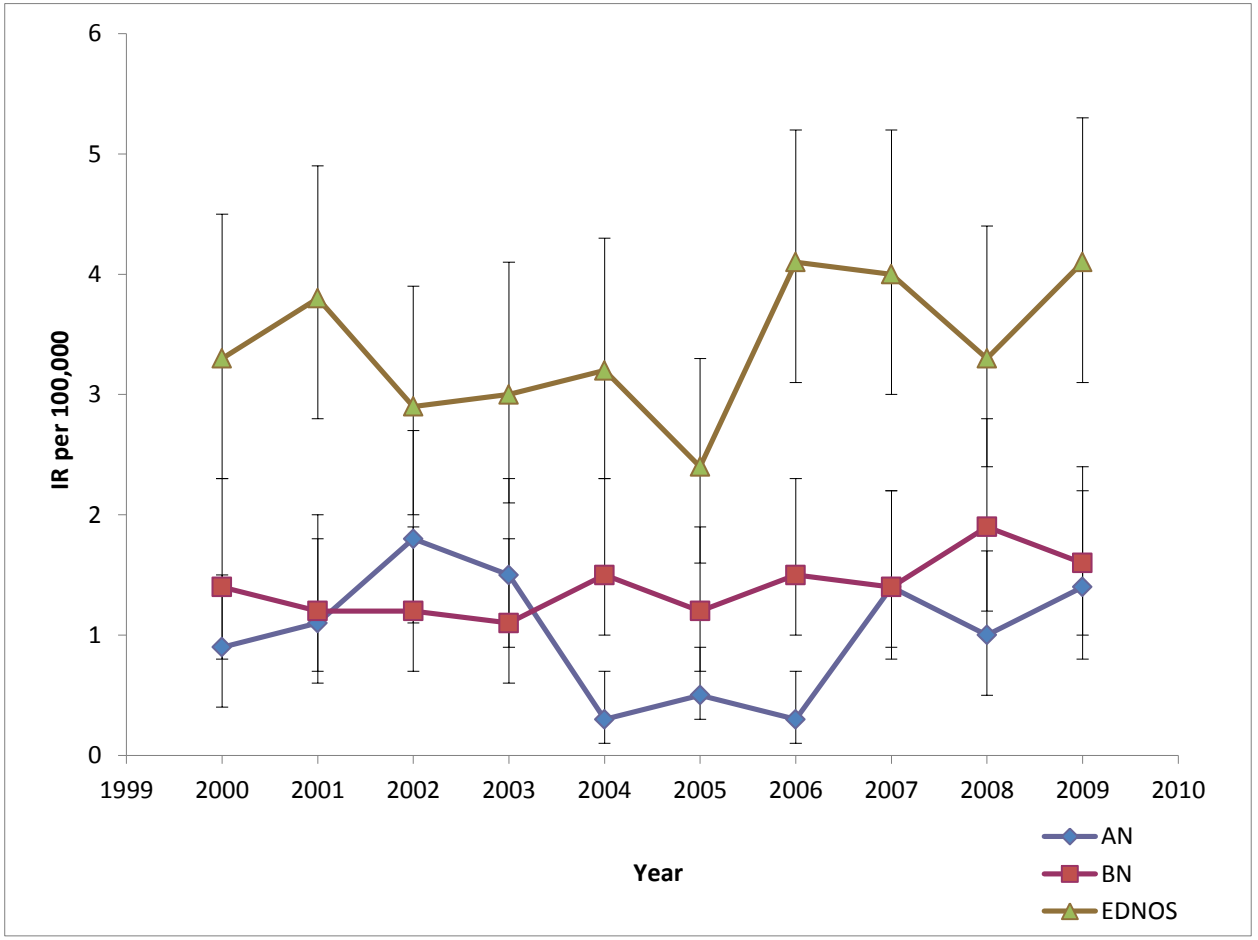
Incidence rates and 95% Confidence Intervals of anorexia nervosa (AN), bulimia nervosa (BN), and eating disorder not otherwise specified (EDNOS) by year for Females aged 10-49



IR: Incidence rate

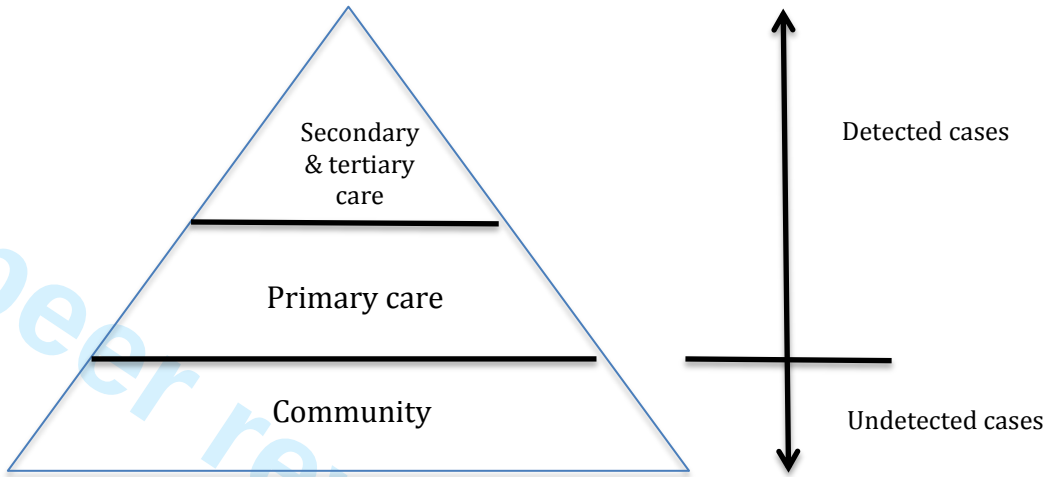
Figure 2

Incidence rates and 95% Confidence Intervals of anorexia nervosa (AN), bulimia nervosa (BN), and eating disorder not otherwise specified (EDNOS) by year for Males aged 10-49



IR: Incidence rate

Figure 3: Incidence of disorders in the community and in the healthcare setting



For peer review only

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	n/a

For Peer Review Only

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only

BMJ open

The Incidence of Eating Disorders in the UK in 2000-2009: findings from the General Practice Research Database

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-002646.R1
Article Type:	Research
Date Submitted by the Author:	18-Mar-2013
Complete List of Authors:	micali, nadia; UCL Institute of Child Health, Hagberg, Katrina; Boston Collaborative Drug Surveillance Program, Boston University School of Public Health, Petersen, Irene; University College London Medical School, Department of Primary Care and Population health Treasure, Janet; King's College London, Institute of Psychiatry, Eating Disorders Research Unit
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Mental health
Keywords:	Eating disorders < PSYCHIATRY, EPIDEMIOLOGY, PRIMARY CARE

SCHOLARONE™
Manuscripts

For peer review only

The Incidence of Eating Disorders in the UK in 2000-2009: findings from the General Practice Research Database

Nadia Micali, MD, PhD, MRCPysch

Behavioural and Brain Sciences Unit, Institute of Child Health, University College London, 30 Guilford Street, WC1N 1EH, UK

Katrina W Hagberg, MPH

Boston Collaborative Drug Surveillance Program, Boston University School of Public Health, Lexington MA 02421 US

Irene Petersen, PhD

Department of Primary Care and Population health, University College London Medical School, Rowland Hill Street London, NW3 2PF

Janet L Treasure , MD, PhD, FRCP, FRCPsych

Eating Disorders Research Unit, Dept. of Psychological Medicine, King's College London, Institute of Psychiatry, London, SE5 8AZ UK

For peer review only

Keywords: epidemiology, incidence, eating disorders, primary care

Word count: 3,056

ABSTRACT

Objectives: Few studies have investigated the incidence of eating disorders (ED). Important questions about changes in incidence of diagnosed disorders in recent years, disorder and gender-specific onset and case detection remain unanswered. Understanding changes in incidence is important for public health, clinical practice and service provision. The aim of this study was to estimate annual (age-, gender-, and subtype-specific) incidence of diagnosed ED: anorexia nervosa, bulimia nervosa and eating disorder not otherwise specified (EDNOS) in primary care over a ten-year period in the UK (2000-2009); to examine changes within the study period; and to describe peak age at diagnosis.

Design: Register-based study.

Setting: Primary care. Data were obtained from a primary care register, the General Practice Research Database, which contains anonymised records representing about 5% of the UK population.

Participants: All patients with a first time diagnosis of anorexia nervosa, bulimia nervosa and EDNOS were identified.

Primary outcome: Annual crude and age-standardized incidence rates were calculated.

Results: A total of 9,062 patients with a first time diagnosis of an ED were identified. The age-standardized annual incidence rate of all diagnosed ED for ages 10-49 increased from 32.3 (95% confidence interval (CI): 31.7-32.9) to 37.2 (95%CI: 36.6-37.9) per 100,000 between 2000 and 2009. The incidence of anorexia and bulimia nervosa was stable; however the incidence of EDNOS increased. The incidence of diagnosed ED was highest for females aged 15-19 and for males aged 10-14.

Conclusions: The age-standardized incidence of ED increased in primary care between 2000 and 2009. New diagnoses of EDNOS increased and EDNOS is the most common eating disorder in primary care.

For peer review only

ARTICLE SUMMARY:

Article focus:

-Determining incidence rates of eating disorders in primary care in the United Kingdom between 2000 and 2009 by age group and gender.

-Investigating changes in incidence of eating disorders between 2009 and 2000.

-Identify age peaks at incidence by gender

Key messages:

-The incidence of eating disorders varied by gender and eating disorder-type. Eating disorder not otherwise specified was the most common incident eating disorder in males and females

- There was a significant increase during the ten years under study in the overall incidence of diagnosed eating disorders both in males and females

-Peak age at diagnosis varied across genders and by eating disorder-type. Adolescent girls aged 15-19 had the highest incidence of eating disorders (2 per 1000).

Strengths and limitations of this study:

-This study is representative of the UK population

-Incidence rates obtained from primary care allow inclusion of all cases presenting to healthcare settings, not just cases presenting to secondary/tertiary care (referral bias)

-However incidence rates obtained in this study are likely to be an underestimate of incident cases present in the community

For peer review only

INTRODUCTION

Eating Disorders (ED) are severe chronic mental health disorders, associated with negative outcomes and the highest mortality amongst psychiatric disorders.[1][2] Understanding changes in their incidence over time and variations by gender and age is important in aiding causal investigations and service provision. Differences across studies in the incidence of EDs have been reported, mainly due to the different populations and nature of the samples studied: primary care registers [3, 4] or community samples.[5, 6] Due to the relatively low incidence rates of ED in the community, studying the incidence of ED at community level is extremely difficult and costly, hence electronic databases and primary care registers can play an important role in understanding changes in the number of individuals developing a disorder and seeking help.

Most studies so far have highlighted consistent incidence rates in primary care (i.e. a stable number of individuals with a new ED diagnosis) for anorexia nervosa (AN) in the 1980s and 1990s, however a recent Dutch study highlighted an increase in the incidence of AN in females aged 15-19 in the 1990s compared to the 1980s.[4] With regards to bulimia nervosa (BN), after an increase in new diagnoses in the 1980s and mid 1990s [3, 7, 8] recent findings have suggested a possible decrease or stabilization since the late 1990s. [3, 4]

Unspecified Eating Disorders, commonly grouped under the “not Otherwise Specified” diagnostic category (EDNOS) have been far less studied than AN and BN. Although EDNOS is the disorder most commonly seen in secondary/tertiary care settings [9, 10] and in general population samples [11] the incidence of EDNOS has not been previously estimated in primary care.

We aimed to: 1. estimate the incidence rates of ED, as well as incidence rates of AN, BN and EDNOS separately, in primary care in the United Kingdom between 2000 and 2009 by age group and gender; 2.

For peer review only

investigate whether the incidence of diagnosed ED changed in 2009 compared to 2000; 3. identify peaks in the incidence of diagnosed ED by gender and age group.

Method:

Sample

We used data from the General Practice Research Database (GPRD), a large automated anonymised UK medical record database containing information from some 400 general practices with cumulative follow-up time of more than 40 million person-years (representing approximately 5% of the general UK population). The general practitioners (GPs) who contribute data to the GPRD use office computers in their routine practice to record medical information including demographic data, medical diagnoses, and deaths in a standard, anonymous format and agree to provide data for research purposes to the GPRD. The practices included are broadly representative of UK general practices in terms of geographic distribution, gender and age of registered patients, and practice size.[12]

The period for this study was 1 January 2000 through 31 December 2009.

We identified all subjects aged 10-49 years for whom data were recorded in the GPRD during the study period.To be eligible for inclusion, patients had to have been registered with the GP for at least 6 months before the first recorded diagnosis and to be 10 to 49 years of age at the time of diagnosis. This age-range was chosen given the very rare number of new onset cases before age 10 and after age 49.[3, 8]

Validity of diagnoses

The comprehensive nature of the information on clinical diagnoses recorded in the GPRD has been repeatedly validated and found to be of high quality for the purpose of conducting epidemiological research [13, 14] (for a systematic review see [15, 16]). In particular ED diagnoses were found to have a positive predictive value of >90% [8, 16], therefore reliable for identifying ED cases.

For peer review only

Case Definition

Patients were identified as incident cases of ED if they had a first time diagnosis of AN, BN or EDNOS recorded in their computerized medical record between 1st January 2000 and 31st December 2009 with no prior recorded ED diagnosis. We used diagnostic codes from a modified version of the Read classification system (Read codes are a standard hierarchical classification system for recording medical information in UK primary care settings) (specific codes available on request).[17,18]

Cases were classified according to the type of ED (AN, BN, or EDNOS) that was recorded.

All cases receiving a diagnosis of EDNOS were identified using the "ED unspecified" code and the "Atypical AN" and "Atypical BN" (codes based on the International Classification of Diseases and Related Health Problems, *tenth revision* - ICD-10,[19] which uses the "Eating Disorder unspecified" notation for EDNOS). EDNOS cases did not have a prior or subsequent diagnosis of either AN or BN within the study period.

Information on weight and height and Body Mass index (BMI) at the time of diagnosis was also evaluated by one of the authors (NM) for 10% of all records (where this information was available in the computerized record) for quality control purposes.

Records of patients who received more than one diagnosis of AN and BN within 3 months were all reviewed by hand and BMI and ED symptoms recorded at the time of diagnosis were used to classify the patient's ED type using an algorithm. Where a patient had a diagnosis of both AN and BN within 3 months and the subject had a BMI and symptoms consistent with one diagnosis (AN or BN) they were considered an incident case of either AN or BN. If the two diagnoses were recorded at least one month apart, and neither BMI nor symptoms were recorded at the time of diagnosis or if BMI or symptoms were consistent with having both AN and BN then the patient was classified as having an incident case of both AN and BN. If the patient received AN and BN diagnoses on the same day and no BMI or symptoms

For peer review only

were recorded we assumed the patient had an ED but could not assign them to AN or BN, therefore they were classified as having EDNOS.

The index date was the date of the first diagnosis of AN, BN, or EDNOS recorded by the GP.

Incidence rates

Total, age-, gender- and year- specific annual incidence rates (IR) of ED diagnoses (all types) and 95% confidence intervals (CI) were calculated. The number of incident cases were divided by the number of subjects aged 10 to 49 registered in GPRD during the calendar year under study (the population at risk). We stratified the annual IRs by age group (10-14, 15-19, 20-29, 30-39 and 40-49 years), gender, and type of ED recorded (AN, BN, or EDNOS).

Age-standardized annual IR for eating disorders were calculated using the direct method, using annual mid-year UK population estimates for the UK data for 2000 and 2009 obtained from the Office of National Statistics (ONS) [20] and 95% confidence intervals were calculated based on the Poisson approximation. Standardised rates were calculated for all and by gender and used to compare changes in recorded incidence between 2000 and 2009 using the *iri* command in Stata 12 (Stata Corp.).

We calculated stratified age and gender specific IR by ED diagnosis for the year 2009.

Ethics

The protocol for this study was reviewed and approved by the Independent Scientific Advisory Committee (ISAC) of the Medicines and Healthcare Products Regulation Agency (MHRA).

For peer review only

Results

We identified 9,120 patients with a first time diagnosis of ED (AN, BN, or EDNOS) recorded in the GPRD during the study period (2000-2009).

Cases with co-occurring diagnoses were reviewed by hand. Among the 69 patients who received a first time diagnosis of AN and BN within a 3 month period, 18 cases were classified as incident cases of AN; 21 were classified as incident cases of BN. In 21 cases both AN and BN diagnoses were plausible and these were considered to have both an incident AN and BN diagnosis. Nine cases received two diagnoses on the same day and these cases were considered to have incident EDNOS.

A total of 2,134 cases (23.5%) were classified as incident cases of AN during the study period; 3,433 cases (37.8%) were considered incident cases of BN; and 3,505 (38.6%) were classified as incident cases of EDNOS.

Annual Incidence Rates

Annual Crude IR of all ED across genders and stratified by gender are shown in the supplemental table (Table S1). The overall crude IR of diagnosed ED was 33.0 (95%CI: 30.7-35.3) in 2000 and 36.8 (95%CI: 34.4-39.2) per 100,000 in 2009. (See table 1).

Age-standardized rates of ED were: 32.3 (95%CI: 31.7-32.9) per 100,000 in 2000 and 37.2 (95%CI: 36.6-37.9) per 100,000 in 2009; showing a statistically significant increase ($p<0.000001$) (see table 1).

Gender-specific Incidence Rates

Females

For peer review only

There was evidence that the overall incidence of ED steadily increased in the period under study for females aged 10-49 (see table S1). The incidence of diagnosed ED in last 3 years of the study period (2007-2009) was higher compared to 2000-2002 with a peak of 63.8 (59.7-68.2) per 100,000 in 2008 (see table S1).

The age-standardised rates of ED in females significantly increased between 2000 and 2009 from 51.8 (95%CI: 50.6-52.9) per 100,000 to 62.6 (95%CI: 61.4-63.8) in 2009 (p<0.00001) (see Table 1).

The incidence of AN in females was stable during the study period despite some minor fluctuations across the years (Figure 1). A formal comparison between the annual IR of diagnosed AN in 2000 and 2009 showed no differences in rates.

The incidence of BN also remained stable during the first decade of the 2000s (see Figure 1).

There was evidence of a steady increase in the incidence of diagnosed EDNOS in females aged 10-49 during the study period. In 2000 the IR was 17.7 (95%CI: 15.5-20.0) per 100,000 compared to 28.4 (95%CI: 25.6-31.4) per 100,000 in 2009 (see Table S1 and Figure 1). There was a significant increase in 2009 compared to 2000 (p<0.00001). During the time under study EDNOS became the most common incident ED diagnosis in females aged 10-49 (figure 1).

Males

The annual crude and age-standardized incidence estimates were similar and increased during the study period (see Table 1). The annual age-standardized incidence of diagnosed ED in males significantly increased from 5.6 (95%CI: 5.3-6.0) per 100,000 in 2000 to 7.1 (95%CI: 6.7-7.5) per 100,000 in 2009 (p<0.00001).

For peer review only

The incidence of diagnosed AN in males remained stable during the study period (see figure 2). The difference in IR between 2000 and 2009 was not statistically significant.

The incidence of BN in males also remained stable between 2000 and 2009 (see figure 2).

EDNOS was the most common diagnosis in males during the study period with an incidence of 3.4 (95%CI: 2.4-4.7) per 100,000 in 2000 and 4.2 (95%CI: 3.1-5.5) per 100,000 in 2009 (see Table S1), representing a 24% increase from 2000 to 2009.

Age-specific Incidence Rates in 2009

Females

In 2009 the crude IR for diagnosed ED for females aged 10-49 was 62.7 (95%CI: 58.4-67.1) per 100,000 (see Table 1).

The highest incidence of AN, BN and EDNOS was for females between 15 and 19 years of age (see Table 3). In this age range the IR for all diagnosed ED was 164.5 (95%CI: 144.6-186.4) per 100,000 (0.2%) (Table 2). Although the peak age at incident diagnosis for both AN and for BN was 15-19 years, 24.0 (95%CI: 16.3-34.3) per 100,000 girls had an onset of AN between the ages of 10-14 years. In contrast, diagnoses of BN peaked between 15-19 years and IR continued to be elevated for those aged 20-29 years (see table 3).

EDNOS was the most common incident diagnosed ED among females aged 10-49: 28.4 (95% CI: 25.6-31.4) per 100,000 in 2009.

Males

In 2009 the crude IR for diagnosed ED for males aged 10-49 years was 7.1 (95%CI: 5.7-8.8) per 100,000 (see Table S1). The peak age of incidence of diagnosed AN in males was 15-19 years (IR=3.8 per 100,000,

For peer review only

95%CI: 1.4-8.3). Diagnosed BN peaked between ages 20 and 29: 4.7 (95%CI: 2.6-7.8) per 100,000. In contrast to females, EDNOS diagnoses in boys peaked between 10-14 years of age (IR= 15.0 per 100,000, 95%CI: 9.1-23.2). EDNOS was the most common diagnosed ED in males aged 10-49 (IR=4.2 per 100,000, 95%CI: 3.1-5.5) (See Table S1).

In 2009 the female to male ratio was 11.8:1 for AN, 14.9:1 for BN; and 7.7:1 for EDNOS.

Discussion

This is the most comprehensive study of the incidence of eating disorders in primary care to date including ~ 40 million person-years of follow-up. We showed that the annual age-standardized incidence of ED in the UK significantly increased between 2000 and 2009. This increase was due to a higher number of new EDNOS diagnoses in the last third of the decade, whilst the number of new diagnoses of AN and BN remained stable across the study period. The peak age of onset for an ED diagnosis in females was between 15 and 19 years. In this age range the incidence of ED for females was 0.2% of the population in 2009. A slightly different pattern of incident diagnosis was observed for males, with the peak age of onset at 15-19 years for AN, 10-14 years for EDNOS, and 20-29 years of age for BN. Whilst the IR became higher than those of AN and BN over the decade, interestingly IR of EDNOS in males were higher compared to those of AN and BN throughout the decade; suggesting that males more often receive a diagnosis of EDNOS compared to AN and BN in primary care in the UK.

Although the lifetime prevalence of BN has been shown to be roughly double of that of AN (0.5% vs. 0.3%) in males in the general population [21] we found an IR ratio closer to 1 for diagnosed BN and AN in this study. This might suggest males are not being diagnosed with BN in general practice in the UK.

For peer review only

This is the first study to investigate the incidence of all ED, including EDNOS, in primary care. Incidence rates of diagnosed AN in the current study were consistent with previous studies on the incidence of AN in the UK using the GPRD. [3, 8] A study using a primary care sample in the Netherlands highlighted an increased incidence rate of AN among adolescent girls in the 1990s;[4] whilst 15-19 was the peak age at diagnosis of AN in our study, we found an incidence rate for girls in this age group of 49.6 per 100,000 in 2009; lower than the 109.2 per 100,000 person years reported in the Dutch Study during the 1990s.[4]

Despite some indications of a decreasing incidence of BN in the late 1990s, [3, 4] in the 2000s our study suggests a stabilization of incidence since the late 1990s. As suggested by Currin et al. [3] peaks of newly diagnosed cases in the mid and late 1990s probably corresponded to increased recognition and detection of a relatively "new" disorder, which has now stabilized at its true level.

This is to our knowledge the first study to estimate the incidence of EDNOS in primary care. Although this disorder was previously considered as encompassing a group of patients with less severe disorders than the classical AN and BN, recent focus on the impact and epidemiology of EDNOS [10, 22, 23] has highlighted its clinical and public health impact. EDNOS is not only acknowledged as the most prevalent ED in clinical and epidemiological samples [9, 10, 24] but it also is as severe as AN and BN in terms of clinical impact and outcomes.

Our findings of an increase in ED diagnoses over the first decade of the 2000s is consistent with two not-mutually exclusive possible explanations: the increase might be secondary to improved recognition and diagnosis at a primary care level, or a true increase in the number of subjects developing ED.

For peer review only

This possibly explains the highlighted increase in EDNOS diagnoses in the later part of the 2000s, maybe secondary to the increased research carried out on EDNOS resulting in increased awareness to the wider spectrum of ED that do not fit into diagnoses of AN and BN. However increased diagnoses might also result from increased presentations to primary care, due to a true increase in disorders.

Strengths and limitations

The GPRD is one of the largest sources of primary care data in the world. Using such a large and independently collected dataset, largely representative of GP practices in the UK, allowed us to estimate the incidence of presentations in a general practice setting. Access to primary care is universal in the UK, therefore results of this study are generalizable to the UK population. Moreover estimating incidence rates in a primary care setting ensures inclusion of mild cases, who normally would not be referred on to specialist services. Given the nature of GPRD we were unable to systematically ensure all diagnoses met DSM-IV or ICD-10 criteria for ED, however general practitioners incorporate data from secondary or tertiary care in the GPRD electronic records when patients are referred, therefore it is possible that some diagnoses included in the database were in fact made by psychiatrists. Moreover, GP diagnoses of eating disorders (and of mental health disorders) in GPRD have been shown to be highly valid.[15, 16] If patients were misclassified it is likely that the diagnostic subgroup might change but not the total incidence of ED diagnoses. This is likely to be particularly relevant to EDNOS, as this diagnosis has not been previously validated in GPRD.

Given that our incidence rates are derived from primary care diagnoses, they allow ascertainment of "detected" incidence rates rather than community incidence rates (see figure 3) and are a close reflection of healthcare need. There is evidence that true rates might be double or triple of those detected in a healthcare setting. [5, 6]

For peer review only

Conclusions

In summary, the incidence of diagnosed ED in the UK significantly increased between 2009 and 2000. The incidence of AN and BN has remained stable in males and females in the first decade of the 21st century; however the incidence of EDNOS increased.

At the peak age of diagnosis (age 15-19 years), it is estimated that 2 girls per 1000 are likely to be newly diagnosed with an ED in the UK. The incidence in this age group suggests that ED may be the most common new onset mental health disorder in adolescent girls after depression, 11.9 in 1,000 girls aged 15-19 received a diagnosis of depression in GPRD in 2009[25]. In females aged 10-19 the incidence rate of ED is about 9-fold higher than the incidence rate of diagnosed type 1 diabetes in the UK (1.2 per 1,000 for ED vs. 0.26 per 1,000 for type 1 diabetes), and about half that of Type-2 diabetes (3.6 per 1,000).[26]

Future research should clarify whether the increase seen in this study reflects a true community increase or better detection. Our findings have important implications for public health, healthcare provision and understanding the development of eating disorders.

Funding:

This research was funded by a National Institute of Health Research (NIHR) clinician scientist award to Dr N Micali. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

The authors declare that they have no conflict of interest.

Author contributions:

Conception and design: Micali, Treasure

Analysis and interpretation of data and drafting the article: Micali, Hagberg, Treasure, Petersen

Critical revision of the manuscript: Treasure, Hagberg, Petersen

For peer review only

References

1. Arcelus J, Mitchell AJ, Wales, J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders: a Meta analysis of 36 studies. *Arch Gen Psychiatry* 2011;68(7):724-731.
2. Field AE, Sonnenville K, Micali N, et al. Common eating disorders predictive of adverse outcomes are missed by the DSM-IV and DSM-5 classifications. *Pediatrics* 2012;130:e289-e295. doi: 10.1542/peds.2011-3663 Published online 16 July 2012.
3. Currin L, Schmidt U, Treasure J, Jick H. Time trends in eating disorder incidence. *Br J Psychiatry* 2005;186:132-135.
4. Van Son GE, van Hoeken D, Bartelds AI, et al. Time trends in the incidence of eating disorders: a primary care study in the Netherlands. *Int J Eat Disord* 2006;39(7):565-9.
5. Keski-Rahkonen A, Hoek HW, Susser ES, et al. Epidemiology and Course of Anorexia Nervosa in the Community. *Am J Psychiatry* 2007;164(8):1259-1265.
6. Keski-Rahkonen A, Hoek HW, Linna MS, et al. Incidence and outcomes of bulimia nervosa: a nationwide population based study. *Psychol Med* 2009;39(5):823-831.
7. Hoek HW, Bartelds AI, Bosveld JJ, et al. Impact of urbanization on detection rates of eating disorders. *Am J Psychiatry* 1995;152:1272-1278.
8. Turnbull S, Ward A, Treasure J, et al. The demand for eating disorder care. An epidemiological study using the general practice research database. *Br J Psychiatry* 1996;169:705-712.
9. Fairburn CG, Cooper Z, Bohn K, et al. The severity and status of eating disorder NOS: implications for DSM-V. *Behav Res Ther* 2007;45(8):1705-15.
10. Nicholls DE, Lynn R, Viner R. Childhood eating disorders: British national surveillance study. *Br J Psychiatry* 2011;198:295-301.

For peer review only

11. Wade TD, Bergin JL, Tiggemann M, et al. Prevalence and long-term course of lifetime eating disorders in an adult Australian twin cohort. *Aust N Z J Psychiatry* 2006;40(2):121-8.

12. Office for National Statistics. Key Health Statistics from general practice 1996: Series MB6 No1. London: Office for National Statistics; 1998.

13. Jick SS, Kaye JA, Vasilakis-Scaramozza C, et al. Validity of the general practice research database. *Pharmacotherapy* 2003;23:686-9.

14. Jick H, Terris BZ, Derby LE, Jick SS. Further validation of information recorded on a general practitioner based computerized data resource in the UK. *Pharmacoepidemiol Drug Saf*. 1992;1: 347-9.

15. Hammad TA, McAdams MA, Feight A, et al. Determining the predictive value of Read/OXMIS codes to identify incident acute myocardial infaraction in the General Practice Research Database. *Pharmacoepidemiol Drug Saf* 2008;17(12):1197-1201.

16. Herrett E, Thomas SL, Schoonen WM, et al. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol* 2010;69(1):4–14.

17. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60(572):e128-36.

18. Dave' S, **Petersen I**. Creating medical and drug code lists to identify cases in primary care databases. *Pharmacoepidemiol Drug Saf.* 2009 Aug;18(8):704-7World Health Organisation . ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. World Health Organisation: Geneva. 1992

19. Office for National Statistics. Mid-year population estimates. United Kingdom. *Office for National Statistics. Key population and vital statistics series* VS NO 30, PP1 No. 26, 2003.

20. Hudson, J., Hiripi, E., Pope, H.G., & Kessler, R.C. The prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. *Biol Psychiatry* 2007 61(3): 348-358.Fairburn CG, Bohn K. Eating disorder NOS (EDNOS): an example of the

For peer review only

troublesome "not otherwise specified" (NOS) category in DSM-IV. *Beh Res Ther* 2005;43(6):691-701.

21. Hay PJ, Mond J, Buttner P, Darby A. Eating Disorder Behaviors Are Increasing: Findings from Two Sequential Community Surveys in South Australia. *PLoS One* 2008;3(2): e1541.
22. Swanson SA, Crow SJ, Le Grange D, et al. Prevalence and correlates of eating disorders in adolescents. Results from the national comorbidity survey replication and adolescent supplement. *Arch Gen Psychiatry* 2011;68(7):714-23.
23. Wijlaars LP, Nazareth I, Petersen I. Trends in Depression and Antidepressant Prescribing in Children and Adolescents: A Cohort Study in The Health Improvement Network (THIN). *PLoS One* 2012;7(3):e33181.
24. González EL, Johansson S, Wallander MA, Rodríguez LA. Trends in the prevalence and incidence of diabetes in the UK: 1996-2005. *J Epidemiol Community Health* 2009;63(4): 332-6.

For peer review only

18

Table 1: Crude and age-standardized Incidence rates for eating disorders in 2000 and 2009 per 100,000 population

	2000			2009		
	No.	**Crude Incidence (95%CI)**	**Age-standardised Incidence (95%CI)**	**No.**	**Crude Incidence (95%CI)**	**Age-standardised Incidence (95%CI)**
Overall	789	33.0 (30.7-35.3)	32.3 (31.7-32.9)	897	36.8 (34.4-39.2)	37.2 (36.6-37.9)
Females	732	53.2 (49.5-57.2)	51.8 (50.6-52.9)	816	62.7 (58.4-67.1)	62.6 (61.4-63.8)
Males	57	5.6 (4.3-7.2)	5.6 (5.3-6.0)	81	7.1 (5.7-8.8)	7.1 (6.7-7.5)

Table 2: Incidence of ED per 100,000 population for the year 2009 by age and gender

ALL EATING DISORDERS						
Age (years)	Females			Males		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	74	116,476	63.5(50.2-79.3)	21	120,219	17.5 (11.1-26.2)
15-19	239	145,279	164.5 (144.6-186.4)	23	132,375	17.4 (11.3-25.6)
20-29	309	349,163	88.5 (79.4-98.8)	28	277,454	10.1 (6.8-14.4)
30-39	138	338,255	40.8 (34.4-48.0)	6	288,468	2.1 (0.8-4.3)
40-49	56	352,843	15.9 (12.1-20.5)	3	319,724	0.9 (0.2-2.5)

For peer review only

19

Table 3: Incidence of eating disorders per 100,000 population for the year 2009 by age, sex and type of eating disorder

ANOREXIA NERVOSA									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	28	116,476	24.0 (16.3-34.3)	3	120,219	2.5 (0.6-6.8)	31	236,695	13,1 (9.0-18.4)
15-19	69	145,279	47.5 (37.2-59.8)	5	132,375	3.8 (1.4-8.3)	74	277,654	26.7 (21.1-33.3)
20-29	66	349,163	18.9 (14.8-23.9)	5	277,454	1.8 (0.7-4.0)	71	626,617	11.3 (8.9-14.2)
30-39	10	338,255	3.0 (1.5-5.3)	1	288,468	0.3 (0.2-1.7)	11	626,723	1.8 (0.9-3.0)
40-49	4	352,843	1.1 (0.4-2.7)	1	319,724	0.3 (0.1-1.5)	5	672,567	0.7 (0.3-1.6)
10-49	**177**	**1,302,016**	**13.6 (11.7-15.7)**	**15**	**1,138,240**	**1.3 (0.8-2.1)**	**192**	**2,440,256**	**7.9 (6.8-9.0)**
BULIMIA NERVOSA									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence(95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	7	116,476	6.0 (2.6-11.9)	0	120,219	0	7	236,695	2.9 (1.1-5.6)
15-19	68	145,279	46.8 (36.6-58.9)	4	132,375	3.0 (0.9-7.3)	72	277,654	25.9 (20.1-32.4)
20-29	111	349,163	31.8 (26.3-38.1)	13	277,454	4.7 (2.6-7.8)	124	626,617	19.8 (16.4-23.2)
30-39	65	338,255	19.2 (15.0-24.3)	1	288,468	0.3 (0.2-1.7)	66	626,723	10.5 (8.2-13.3)
40-49	18	352,843	5.1 (3.1-7.9)	0	319,724	0	18	672,567	2.7 (1.6-3.8)
10-49	**269**	**1,302,016**	**20.7 (18.3-23.2)**	**18**	**1,138,240**	**1.6 (1.0-2.4)**	**287**	**2,440,256**	**11.8 (10.5-13.2)**
EATING DISORDER NOS (EDNOS)									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	39	116,476	33.5 (24.1-45.3)	18	120,219	15.0 (9.1-23.2)	57	236,695	24.1 (18.4-31.0)
15-19	102	145,279	70.2 (57.5-84.9)	14	132,375	10.6 (6.0-17.3)	116	277,654	41.8 (34.7-49.9)
20-29	132	349,163	37.8 (31.8-44.7)	9	277,454	3.2 (1.6-5.9)	142	626,617	22.7 (19.2-26.6)
30-39	63	338,255	18.6 (14.4-23.7)	4	288,468	1.4 (0.4-3.3)	67	626,723	10.7 (8.3-13.5)
40-49	34	352,843	9.6 (6.8-13.3)	2	319,724	0.6 (0.1-2.0)	36	672,567	5.3 (3.8-7.3)
10-49	**370**	**1,302,016**	**28.4 (25.6-31.4)**	**48**	**1,138,240**	**4.2 (3.1-5.5)**	**418**	**2,440,256**	**17.1 (15.5-18.8)**

For peer review only

The Incidence of Eating Disorders in the UK in 2000-2009: findings from the General Practice Research Database

Nadia Micali, MD, PhD, MRCPysch

Behavioural and Brain Sciences Unit, Institute of Child Health, University College London, 30 Guilford Street, WC1N 1EH, UK

Katrina W Hagberg, MPH

Boston Collaborative Drug Surveillance Program, Boston University School of Public Health, Lexington MA 02421 US

Irene Petersen, PhD

Department of Primary Care and Population health, University College London Medical School, Rowland Hill Street London, NW3 2PF

Janet L Treasure , MD, PhD, FRCP, FRCPsych

Eating Disorders Research Unit, Dept. of Psychological Medicine, King's College London, Institute of Psychiatry, London, SE5 8AZ UK

Keywords: epidemiology, incidence, eating disorders, primary care

Word count: 3,056

Formatted: Section start: Continuous

For peer review only

ABSTRACT

Objectives: Few studies have investigated the incidence of eating disorders (ED). Important questions about changes in incidence of diagnosed disorders in recent years, disorder and gender-specific onset and case detection remain unanswered. Understanding changes in incidence is important for public health, clinical practice and service provision. The aim of this study was to estimate annual (age-, gender-, and subtype-specific) incidence of diagnosed ED: anorexia nervosa, bulimia nervosa and eating disorder not otherwise specified (EDNOS) in primary care over a ten-year period in the UK (2000-2009); to examine changes within the study period; and to describe peak age at diagnosis.

Design: Register-based study.

Setting: Primary care. Data were obtained from a primary care register, the General Practice Research Database, which contains anonymised records representing about 5% of the UK population.

Participants: All patients with a first time diagnosis of anorexia nervosa, bulimia nervosa and EDNOS were identified.

Primary outcome: Annual crude and age-standardized incidence rates were calculated.

Results: A total of 9,062 patients with a first time diagnosis of an ED were identified. The age-standardized annual incidence rate of all diagnosed ED for ages 10-49 increased from 32.3 (95% confidence interval (CI): 31.7-32.9) to 37.2 (95%CI: 36.6-37.9) per 100,000 between 2000 and 2009. The incidence of anorexia and bulimia nervosa was stable; however the incidence of EDNOS increased. The incidence of diagnosed ED was highest for females aged 15-19 and for males aged 10-14.

Conclusions: The age-standardized incidence of ED increased in primary care between 2000 and 2009. New diagnoses of EDNOS increased and EDNOS is the most common eating disorder in primary care.

Formatted: Section start: Continuous, Different first page header

For peer review only

3

ARTICLE SUMMARY:

Article focus:

-Determining incidence rates of eating disorders in primary care in the United Kingdom between 2000 and 2009 by age group and gender.

-Investigating changes in incidence of eating disorders between 2009 and 2000.

-Identify age peaks at incidence by gender

Key messages:

-The incidence of eating disorders varied by gender and eating disorder-type. Eating disorder not otherwise specified was the most common incident eating disorder in males and females

- There was a significant increase during the ten years under study in the overall incidence of diagnosed eating disorders both in males and females

-Peak age at diagnosis varied across genders and by eating disorder-type. Adolescent girls aged 15-19 had the highest incidence of eating disorders (2 per 1000).

Strengths and limitations of this study:

-This study is representative of the UK population

-Incidence rates obtained from primary care allow inclusion of all cases presenting to healthcare settings, not just cases presenting to secondary/tertiary care (referral bias)

-However incidence rates obtained in this study are likely to be an underestimate of incident ca~~e~~ses present in the community

For peer review only

INTRODUCTION

Eating Disorders (ED) are severe chronic mental health disorders, associated with negative outcomes and the highest mortality amongst psychiatric disorders.[1][2] Understanding changes in their incidence over time and variations by gender and age is important in aiding causal investigations and service provision. Differences across studies in the incidence of EDs have been reported, mainly due to the different populations and nature of the samples studied: primary care registers [3, 4] or community samples.[5, 6] Due to the relatively low incidence rates of ED in the community, studying the incidence of ED at community level is extremely difficult and costly, hence electronic databases and primary care registers can play an important role in understanding changes in the number of individuals developing a disorder and seeking help.

Most studies so far have highlighted consistent incidence rates in primary care (i.e. a stable number of individuals with a new ED diagnosis) for anorexia nervosa (AN) in the 1980s and 1990s, however a recent Dutch study highlighted an increase in the incidence of AN in females aged 15-19 in the 1990s compared to the 1980s.[4] With regards to bulimia nervosa (BN), after an increase in new diagnoses in the 1980s and mid 1990s [3, 7, 8] recent findings have suggested a possible decrease or stabilization since the late 1990s. [3, 4]

Unspecified Eating Disorders, commonly grouped under the “not Otherwise Specified” diagnostic category (EDNOS) have been far less studied than AN and BN. Although EDNOS is the disorder most commonly seen in secondary/tertiary care settings [9, 10] and in general population samples [11] the incidence of EDNOS has not been previously estimated in primary care.

We aimed to: 1. estimate the incidence rates of ED, as well as incidence rates of AN, BN and EDNOS separately, in primary care in the United Kingdom between 2000 and 2009 by age group and gender; 2.

For peer review only

investigate whether the incidence of diagnosed ED changed in 2009 compared to 2000; 3. identify peaks in the incidence of diagnosed ED by gender and age group.

Method:

Sample

We used data from the General Practice Research Database (GPRD), a large automated anonymised UK medical record database containing information from some 400 general practices with cumulative follow-up time of more than 40 million person-years (representing approximately 5% of the general UK population). ~~The comprehensive nature of the information on clinical diagnoses and drug exposure recorded in the GPRD has been repeatedly validated and found to be of high quality for the purpose of conducting epidemiological research.[12, 13]~~ The general practitioners (GPs) who contribute data to the GPRD use office computers in their routine practice to record medical information including demographic data, medical diagnoses, and deaths in a standard, anonymous format and agree to provide data for research purposes to the GPRD. The practices included are broadly representative of UK general practices in terms of geographic distribution, gender and age of registered patients, and practice size.[124]

The period for this study was 1 January 2000 through 31 December 2009.

We identified all subjects aged 10-49 years for whom data were recorded in the GPRD during the study period.To be eligible for inclusion, patients had to have been registered with the GP for at least 6 months before the first recorded diagnosis and to be 10 to 49 years of age at the time of diagnosis. This age-range was chosen given the very rare number of new onset cases before age 10 and after age 49.[3, 8]

Validity of diagnoses

The comprehensive nature of the information on clinical diagnoses recorded in the GPRD has been repeatedly validated and found to be of high quality for the purpose of conducting epidemiological

For peer review only

6

research [132, 143] (for a systematic review see [156, 167]). In particular ED diagnoses were found to have a positive predictive value of >90% [8, 167], therefore reliable for identifying ED cases.

~~The period for this study was 1 January 2000 through 31 December 2009.~~

~~We identified all subjects aged 10-49 years for whom data were recorded in the GPRD during the study period.~~

~~To be eligible for inclusion, patients had to have been registered with the GP for at least 6 months before the first recorded diagnosis and to be 10 to 49 years of age at the time of diagnosis. This age-range was chosen given the very rare number of new onset cases before age 10 and after age 49.[3, 8]~~

Case Definition

Patients were identified as incident cases of ED if they had a first time diagnosis of AN, BN or EDNOS recorded in their computerized medical record between 1st January 2000 and 31st December 2009 with no prior recorded ED diagnosis. We used diagnostic codes from a modified version of the Read classification system (Read codes are a standard hierarchical classification system for recording medical information in UK primary care settings) (specific codes available on request).[17,185] ~~To be eligible for inclusion, patients had to have been registered with the GP for at least 6 months before the first recorded diagnosis and to be 10 to 49 years of age at the time of diagnosis. This age-range was chosen given the very rare number of new onset cases before age 10 and after age 49.[3, 8] Information on weight and height and Body Mass index (BMI) at the time of diagnosis was also evaluated by one of the authors (NM) for 10% of all records (where this information was available in the computerized record).~~

Cases were classified according to the type of ED (AN, BN, or EDNOS) that was recorded.

All cases receiving a diagnosis of EDNOS were identified using the "ED unspecified" code and the "Atypical AN" and "Atypical BN" (codes based on the International Classification of Diseases and Related

Formatted: Don't adjust space between Latin and Asian text, Don't adjust space between Asian text and numbers

Formatted: Font: +Headings (Calibri)

Formatted: Font: +Headings (Calibri), 12 pt

Formatted: Font: +Headings (Calibri), 12 pt

Formatted: Font: (Default) AdvP41153C, 11 pt, Font color: Custom Color(RGB(35,31,32)), English (U.K.)

For peer review only

7

Health Problems, *tenth revision* - ICD-10,[196] which uses the "Eating Disorder unspecified" notation for EDNOS). EDNOS cases did not have a prior or subsequent diagnosis of either AN or BN within the study period.

Information on weight and height and Body Mass index (BMI) at the time of diagnosis was also evaluated by one of the authors (NM) for 10% of all records (where this information was available in the computerized record) for quality control purposes.

Records of patients who received more than one diagnosis of AN and BN within 3 months were all reviewed by hand and BMI and ED symptoms recorded at the time of diagnosis were used to classify the patient's ED type using an algorithm. ~~In instances~~ Wwhere a patient had a diagnosis of both AN and BN within 3 months and the subject had a BMI and symptoms consistent with one diagnosis ~~only~~ (AN or BN) ~~at the time of diagnosis~~ they were considered an incident case of either AN or BN. If the two diagnoses were recorded at least one month apart, and neither BMI nor symptoms were recorded at the time of diagnosis ~~and the two diagnoses were recorded at least one month apart~~ or if BMI or symptoms were consistent with having both AN and BN then the patient was classified as having an incident case of both AN and BN. If the patient received AN and BN diagnoses on the same day and no BMI or symptoms were recorded we assumed the patient had an ED but could not assign them to AN or BN, therefore they were classified as having EDNOS.

The index date was the date of the first diagnosis of AN, BN, or EDNOS recorded by the GP.

Incidence rates

Total, age-, gender- and year- specific annual incidence rates (IR) of ED diagnoses (all types) and 95% confidence intervals (CI) were calculated. The number of incident cases were divided by the number of subjects aged 10 to 49 registered in GPRD during the calendar year under study (the population at risk).

For peer review only

8

We stratified the annual IRs by age group (10-14, 15-19, 20-29, 30-39 and 40-49 years), gender, and type of ED recorded (AN, BN, or EDNOS).

Age-standardized annual IR for eating disorders were calculated using the direct method, using annual mid-year UK population estimates for the UK data for 2000 and 2009 obtained from the Office of National Statistics (ONS) [20] and 95% confidence intervals were calculated based on the Poisson approximation. Standardised rates were calculated for all and by gender and used to compare changes in recorded incidence between 2000 and 2009 using the *iri* command in Stata 12 (Stata Corp.).

We calculated stratified age and gender specific IR by ED diagnosis for the year 2009.

Ethics

The protocol for this study was reviewed and approved by the Independent Scientific Advisory Committee (ISAC) of the Medicines and Healthcare Products Regulation Agency (MHRA).

Results

We identified 9,120~~062~~ patients with a first time diagnosis of ED (AN, BN, or EDNOS) recorded in the GPRD during the study period (2000-2009).

Cases with co-occurring diagnoses were reviewed by hand. Among the 69~~73~~ patients who received a first time diagnosis of AN and BN within a 3 month period, 18 cases were classified as incident cases of AN; 2~~13~~ were classified as incident cases of BN. In 2~~15~~ cases both AN and BN diagnoses were plausible and

For peer review only

these were considered to have both an incident AN and BN diagnosis. Nine ~~Seven~~ cases received two diagnoses on the same day and these cases were considered to have incident EDNOS.

A total of 2,134 cases (23.5%) were classified as incident cases of AN during the study period; 3,433 cases (37.8%) were considered incident cases of BN; and 3,505 (38.6%) were classified as incident cases of EDNOS.

Annual Incidence Rates

Annual Crude IR of all ED across genders and stratified by gender are shown in the supplemental table (Table S1). The overall crude IR of diagnosed ED was 33.0 (95%CI: 30.7-35.3) in 2000 and 36.8 (95%CI: 34.4-39.2) per 100,000 in 2009. (See table 1).

Age-standardized rates of ED were: 32.3 (95%CI: 31.7-32.9) per 100,000 in 2000 and 37.2 (95%CI: 36.6-37.9) per 100,000 in 2009; showing a statistically significant increase (p<0.000001) (see table 1).

Gender-specific Incidence Rates

Females

There was evidence that the overall incidence of ~~all~~ ED steadily increased in the period under study for females aged 10-49 (see table S~~Figure~~ 1). The incidence of diagnosed ED in last 3 years of the study period (2007-2009) was higher compared to 2000-2002 with a peak of 63.8 (59.7-68.2) per 100,000 in 2008 (see table S1).

The age-standardised rates of ED in females significantly increased between 2000 and 2009 from 51.8 (95%CI: 50.6-52.9) per 100,000 to 62.6 (95%CI: 61.4-63.8) in 2009 (p<0.00001) (see Table 1).

For peer review only

10

The incidence of AN in females was stable during the study period despite some minor fluctuations across the years (Figure 1). A formal comparison between the annual IR of diagnosed AN in 2000 and 2009 showed no differences in rates.

The incidence of BN also remained stable during the first decade of the 2000s (see Figure 1).

There was evidence of a steady increase in the incidence of diagnosed EDNOS in females aged 10-49 during the study period. In 2000 the IR was 17.74 (95%CI: 15.53-20.0) per 100,000 compared to 28.47.6 (95%CI: 25.64.9-31.40.6) per 100,000 in 2009 (see Table S1 and Figure 1). There was a significant increase in 2009 compared to 2000 (p<0.00001). During the time under study EDNOS became the most common incident ED diagnosis in females aged 10-49 (figure 1).

Males

The annual crude and age-standardized incidence estimates were similar and increased during the study period (see Table 1). The annual age-standardized incidence of diagnosed ED in males significantly increased from 5.6 (95%CI: 5.3-6.0) per 100,000 in 2000 to 7.1 (95%CI: 6.7-7.5) per 100,000 in 2009 (p<0.00001).

The incidence of diagnosed AN in males remained stable during the study period (see figure 2). The difference in IR between 2000 and 2009 was not statistically significant.

The incidence of BN in males also remained stable between 2000 and 2009 (see figure 2).

EDNOS was the most common diagnosis in males during the study period with an incidence of 3.43 (95%CI: 2.43-4.75) per 100,000 in 2000 and 4.21 (95%CI: 3.1-5.53) per 100,000 in 2009 (see Table S1), representing a 24% increase from 2000 to 2009.

For peer review only

11

Age-specific Incidence Rates in 2009

Females

In 2009 the crude IR for diagnosed ED for females aged 10-49 was 62.7 (95%CI: 58.4-67.1) per 100,000 (see Table 1).

The highest incidence of AN, BN and EDNOS was for females between 15 and 19 years of age (see Table 3). In this age range the IR for all diagnosed ED was 164.5 (95%CI: 144.6-186.4) per 100,000 (0.2%) (Table 2). Although the peak age at incident diagnosis for both AN and for BN was 15-19 years, 24.0 (95%CI: 16.3-34.3) per 100,000 girls had an onset of AN between the ages of 10-14 years. In contrast, diagnoses of BN peaked between 15-19 years and IR continued to be elevated for those aged 20-29 years (see table 3).

EDNOS was the most common incident diagnosed ED among females aged 10-49: 28.4 (95% CI: 25.6-31.4)~~27.6 (95% CI: 24.9-30.6)~~ per 100,000 in 2009.

Formatted: Font: 12 pt, Not Bold, Not Highlight

Formatted: Font: 12 pt, Not Bold, Not Highlight

Males

In 2009 the crude IR for diagnosed ED for males aged 10-49 years was 7.1 (95%CI: 5.7-8.8) per 100,000 (see Table S1). The peak age of incidence of diagnosed AN in males was 15-19 years (IR=3.8 per 100,000, 95%CI: 1.4-8.3). Diagnosed BN peaked between ages 20 and 29: 4.7 (95%CI: 2.6-7.8) per 100,000. In contrast to females, EDNOS diagnoses in boys peaked between 10-14 years of age (IR= 15.0 per 100,000, 95%CI: 9.1-23.2). EDNOS was the most common diagnosed ED in males aged 10-49 (IR=4.2~~1~~ per 100,000, 95%CI: 3.1-5.5~~4~~) (See Table S1).

In 2009 the female to male ratio was 11.8:1 for AN, 14.9:1 for BN; and 7.7:1 for EDNOS.

For peer review only

12

Discussion

This is the most comprehensive study of the incidence of eating disorders in primary care to date including ~ 40 million person-years of follow-up. We showed that the annual age-standardized incidence of ED in the UK significantly increased between 2000 and 2009. This increase was due to a higher number of new EDNOS diagnoses in the last third of the decade, whilst the number of new diagnoses of AN and BN remained stable across the study period. The peak age of onset for an ED diagnosis in females was between 15 and 19 years. In this age range the incidence of ED for females was 0.2% of the population in 2009. A slightly different pattern of incident diagnosis was observed for males, with the peak age of onset at 15-19 years for AN, 10-14 years for EDNOS, and 20-29 years of age for BN. Whilst the IR became higher than those of AN and BN over the decade, interestingly IR of EDNOS in males were higher compared to those of AN and BN throughout the decade; suggesting that males more often receive a diagnosis of EDNOS compared to AN and BN in primary care in the UK.

Although the lifetime prevalence of BN has been shown to be roughly double of that of AN (0.5% vs. 0.3%) in males in the general population [21.] we found an IR ratio closer to 1 for diagnosed BN and AN in this study. This might suggest males are not being diagnosed with BN in general practice in the UK.

This is the first study to investigate the incidence of all ED, including EDNOS, in primary care. Incidence rates of diagnosed AN in the current study were consistent with previous studies on the incidence of AN in the UK using the GPRD. [3, 8] A study using a primary care sample in the Netherlands highlighted an increased incidence rate of AN among adolescent girls in the 1990s;[4] whilst 15-19 was the peak age at diagnosis of AN in our study, we found an incidence rate for girls in this age group of 49.6 per 100,000 in 2009; lower than the 109.2 per 100,000 person years reported in the Dutch Study during the 1990s.[4]

For peer review only

13

Despite some indications of a decreasing incidence of BN in the late 1990s, [3, 4] in the 2000s our study suggests a stabilization of incidence since the late 1990s. As suggested by Currin et al. [3] peaks of newly diagnosed cases in the mid and late 1990s probably corresponded to increased recognition and detection of a relatively "new" disorder, which has now stabilized at its true level.

This is to our knowledge the first study to estimate the incidence of EDNOS in primary care. Although this disorder was previously considered as encompassing a group of patients with less severe disorders than the classical AN and BN, recent focus on the impact and epidemiology of EDNOS [10, 2219, 230] has highlighted its clinical and public health impact. EDNOS is not only acknowledged as the most prevalent ED in clinical and epidemiological samples [9, 10, 241] but it also is as severe as AN and BN in terms of clinical impact and outcomes.

Our findings of an increase in ED diagnoses over the first decade of the 2000s is consistent with two not-mutually exclusive possible explanations: the increase might be secondary to improved recognition and diagnosis at a primary care level, or a true increase in the number of subjects developing ED.

This possibly explains the highlighted increase in EDNOS diagnoses in the later part of the 2000s, maybe secondary to the increased research carried out on EDNOS resulting in increased awareness to the wider spectrum of ED that do not fit into diagnoses of AN and BN. However increased diagnoses might also result from increased presentations to primary care, due to a true increase in disorders.

Strengths and limitations

The GPRD is one of the largest sources of primary care data in the world. Using such a large and independently collected dataset, largely representative of GP practices in the UK, allowed us to estimate

For peer review only

the incidence of presentations in a general practice setting. Access to primary care is universal in the UK, therefore results of this study are generalizable to the UK population. Moreover estimating incidence rates in a primary care setting ensures inclusion of mild cases, who normally would not be referred on to specialist services. Given the nature of GPRD we were unable to systematically ensure all diagnoses met DSM-IV or ICD-10 criteria for ED, however general practitioners incorporate data from secondary or tertiary care in the GPRD electronic records when patients are referred, therefore it is possible that some diagnoses included in the database were in fact made by psychiatrists. Moreover, GP diagnoses of eating disorders (and of mental health disorders) in GPRD have been shown to be highly valid.[158, 169] If patients were misclassified it is likely that the diagnostic subgroup might change but not the total incidence of ED diagnoses. This is likely to be particularly relevant to EDNOS, as this diagnosis has not been previously validated in GPRD.

Given that our incidence rates are derived from primary care diagnoses, they allow ascertainment of "detected" incidence rates rather than community incidence rates (see figure 3) and are a close reflection of healthcare need. There is evidence that true rates might be double or triple of those detected in a healthcare setting. [5, 6]

Conclusions

In summary, the incidence of diagnosed ED in the UK significantly increased between 2009 and 2000. The incidence of AN and BN has remained stable in males and females in the first decade of the 21st century; however the incidence of EDNOS increased.

At the peak age of diagnosis (age 15-19 years), it is estimated that 2 girls per 1000 are likely to be newly diagnosed with an ED in the UK. The incidence in this age group suggests that ED may be the most common new onset mental health disorder in adolescent girls after depression, 11.9 in 1,000 girls aged 15-19 received a diagnosis of depression in GPRD in 2009[252]. In females aged 10-19 the incidence rate

For peer review only

15

of ED is about 9-fold higher than the incidence rate of diagnosed type 1 diabetes in the UK (1.2 per 1,000 for ED vs. 0.26 per 1,000 for type 1 diabetes), and about half that of Type-2 diabetes (3.6 per 1,000).[2~~6~~3]

Future research should clarify whether the increase seen in this study reflects a true community increase or better detection. Our findings have important implications for public health, healthcare provision and understanding the development of eating disorders.

Funding:

This research was funded by a National Institute of Health Research (NIHR) clinician scientist award to Dr N Micali. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

The authors declare that they have no conflict of interest.

Author contributions:

Conception and design: Micali, Treasure

Analysis and interpretation of data and drafting the article: Micali, Hagberg, Treasure, Petersen

Critical revision of the manuscript: Treasure, Hagberg, Petersen

Formatted: Body Text 2, Line spacing: single

For peer review only

16

References

1. Arcelus J, Mitchell AJ, Wales, J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders: a Meta analysis of 36 studies. *Arch Gen Psychiatry* 2011;68(7):724-731.
2. Field AE, Sonnenville K, Micali N, et al. Common eating disorders predictive of adverse outcomes are missed by the DSM-IV and DSM-5 classifications. *Pediatrics* 2012;130:e289-e295. doi: 10.1542/peds.2011-3663 Published online 16 July 2012.
3. Currin L, Schmidt U, Treasure J, Jick H. Time trends in eating disorder incidence. *Br J Psychiatry* 2005;186:132-135.
4. Van Son GE, van Hoeken D, Bartelds AI, et al. Time trends in the incidence of eating disorders: a primary care study in the Netherlands. *Int J Eat Disord* 2006;39(7):565-9.
5. Keski-Rahkonen A, Hoek HW, Susser ES, et al. Epidemiology and Course of Anorexia Nervosa in the Community. *Am J Psychiatry* 2007;164(8):1259-1265.
6. Keski-Rahkonen A, Hoek HW, Linna MS, et al. Incidence and outcomes of bulimia nervosa: a nationwide population based study. *Psychol Med* 2009;39(5):823-831.
7. Hoek HW, Bartelds AI, Bosveld JJ, et al. Impact of urbanization on detection rates of eating disorders. *Am J Psychiatry* 1995;152:1272-1278.
8. Turnbull S, Ward A, Treasure J, et al. The demand for eating disorder care. An epidemiological study using the general practice research database. *Br J Psychiatry* 1996;169:705-712.
9. Fairburn CG, Cooper Z, Bohn K, et al. The severity and status of eating disorder NOS: implications for DSM-V. *Behav Res Ther* 2007;45(8):1705-15.
10. Nicholls DE, Lynn R, Viner R. Childhood eating disorders: British national surveillance study. *Br J Psychiatry* 2011;198:295-301.

For peer review only

17

11. Wade TD, Bergin JL, Tiggemann M, et al. Prevalence and long-term course of lifetime eating disorders in an adult Australian twin cohort. *Aust N Z J Psychiatry* 2006;40(2):121-8.

12. Office for National Statistics. Key Health Statistics from general practice 1996: Series MB6 No1. London: Office for National Statistics; 1998.

13. Jick SS, Kaye JA, Vasilakis-Scaramozza C, et al. Validity of the general practice research database. *Pharmacotherapy* 2003;23:686-9.

14. Jick H, Terris BZ, Derby LE, Jick SS. Further validation of information recorded on a general practitioner based computerized data resource in the UK. *Pharmacoepidemiol Drug Saf*. 1992;1: 347-9.

15. Hammad TA, McAdams MA, Feight A, et al. Determining the predictive value of Read/OXMIS codes to identify incident acute myocardial infaraction in the General Practice Research Database. *Pharmacoepidemiol Drug Saf* 2008;17(12):1197-1201.

16. Herrett E, Thomas SL, Schoonen WM, et al. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol* 2010;69(1):4–14.

17. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60(572):e128-36.

18. Dave' S, **Petersen I**. Creating medical and drug code lists to identify cases in primary care databases. *Pharmacoepidemiol Drug Saf.* 2009 Aug;18(8):704-7~~Jick SS, Kaye JA, Vasilakis-Scaramozza C, et al. Validity of the general practice research database. *Pharmacotherapy* 2003;23:686-9.~~

19. World Health Organisation . ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. World Health Organisation: Geneva. 1992

20. Office for National Statistics. Mid-year population estimates. United Kingdom. *Office for National Statistics. Key population and vital statistics series* VS NO 30, PP1 No. 26, 2003.

For peer review only

18

~~20.~~21. Hudson, J., Hiripi, E., Pope, H.G., & Kessler, R.C. The prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. *Biol Psychiatry* 2007 61(3): 348-358.~~Office for National Statistics. Key Health Statistics from general practice 1996: Series MB6 No1. London: Office for National Statistics; 1998.~~

22. Fairburn CG, Bohn K. Eating disorder NOS (EDNOS): an example of the troublesome "not otherwise specified" (NOS) category in DSM-IV. *Beh Res Ther* 2005;43(6):691-701.

~~21.~~23. Hay PJ, Mond J, Buttner P, Darby A. Eating Disorder Behaviors Are Increasing: Findings from Two Sequential Community Surveys in South Australia. *PLoS One* 2008;3(2): e1541.

~~22.~~24. Swanson SA, Crow SJ, Le Grange D, et al. Prevalence and correlates of eating disorders in adolescents. Results from the national comorbidity survey replication and adolescent supplement. *Arch Gen Psychiatry* 2011;68(7):714-23.

~~23.~~25. Wijlaars LP, Nazareth I, Petersen I. Trends in Depression and Antidepressant Prescribing in Children and Adolescents: A Cohort Study in The Health Improvement Network (THIN). *PLoS One* 2012;7(3):e33181.

~~24.~~26. González EL, Johansson S, Wallander MA, Rodríguez LA. Trends in the prevalence and incidence of diabetes in the UK: 1996-2005. *J Epidemiol Community Health* 2009;63(4): 332-6.

~~25. Hammad TA, McAdams MA, Feight A, et al. Determining the predictive value of Read/OXMIS codes to identify incident acute myocardial infaraction in the General Practice Research Database. *Pharmacoepidemiol Drug Saf* 2008;17(12):1197-1201.~~

Formatted: Font: Italic, English (U.K.)

Formatted: Indent: Left: 0.5", No bullets or numbering

Formatted: Font: +Headings (Calibri)

Formatted: Indent: Left: 0.5", Line spacing: Double, No bullets or numbering

For peer review only

19

26.27. World Health Organisation: ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines.-World Health Organisation: Geneva. 1992.

27. Office for National Statistics. Mid-year population estimates. United Kingdom. *Office for National Statistics. Key population and vital statistics series* VS NO 30, PP1 No. 26, 2003. Herrett E, Thomas SL, Schoonen WM, et al. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol* 2010;69(1):4–14.

28. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60(572):e128–36.

29. Fairburn CG, Bohn K. Eating disorder NOS (EDNOS): an example of the troublesome "not otherwise specified" (NOS) category in DSM-IV. *Beh Res Ther* 2005;43(6):691–701.

30.29. Hay PJ, Mond J, Buttner P, Darby A. Eating Disorder Behaviors Are Increasing: Findings from Two Sequential Community Surveys in South Australia. *PLoS One* 2008;3(2): e1541.

31.30. Swanson SA, Crow SJ, Le Grange D, et al. Prevalence and correlates of eating disorders in adolescents. Results from the national comorbidity survey replication and adolescent supplement. *Arch Gen Psychiatry* 2011;68(7):714–23.

32.31. Wijlaars LP, Nazareth I, Petersen I. Trends in Depression and Antidepressant Prescribing in Children and Adolescents: A Cohort Study in The Health Improvement Network (THIN). *PLoS One* 2012;7(3):e33181.

33.32. González EL, Johansson S, Wallander MA, Rodríguez LA. Trends in the prevalence and incidence of diabetes in the UK: 1996–2005. *J Epidemiol Community Health* 2009;63(4): 332–6.

Formatted: Font: (Default) Calibri

Formatted: desc, Line spacing: single

Formatted: Font: (Default) Times New Roman

For peer review only

20

Table 1: Crude and age-standardized Incidence rates for eating disorders in 2000 and 2009 per 100,000 population

	2000			2009		
	No.	**Crude Incidence (95%CI)**	**Age-standardised Incidence (95%CI)**	**No.**	**Crude Incidence (95%CI)**	**Age-standardised Incidence (95%CI)**
Overall	789	33.0 (30.7-35.3)	32.3 (31.7-32.9)	897	36.8 (34.4-39.2)	37.2 (36.6-37.9)
Females	732	53.2 (49.5-57.2)	51.8 (50.6-52.9)	816	62.7 (58.4-67.1)	62.6 (61.4-63.8)
Males	57	5.6 (4.3-7.2)	5.6 (5.3-6.0)	81	7.1 (5.7-8.8)	7.1 (6.7-7.5)

Table 2: Incidence of ED per 100,000 population for the year 2009 by age and gender

ALL EATING DISORDERS						
Age (years)	Females			Males		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	74	116,476	63.5(50.2-79.3)	21	120,219	17.5 (11.1-26.2)
15-19	239	145,279	164.5 (144.6-186.4)	23	132,375	17.4 (11.3-25.6)
20-29	309	349,163	88.5 (79.4-98.8)	28	277,454	10.1 (6.8-14.4)
30-39	138	338,255	40.8 (34.4-48.0)	6	288,468	2.1 (0.8-4.3)
40-49	56	352,843	15.9 (12.1-20.5)	3	319,724	0.9 (0.2-2.5)

Formatted: Section start: Continuous

For peer review only

21

Table 3: Incidence of eating disorders per 100,000 population for the year 2009 by age, sex and type of eating disorder

ANOREXIA NERVOSA									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	28	116,476	24.0 (16.3-34.3)	3	120,219	2.5 (0.6-6.8)	31	236,695	13,1 (9.0-18.4)
15-19	69	145,279	47.5 (37.2-59.8)	5	132,375	3.8 (1.4-8.3)	74	277,654	26.7 (21.1-33.3)
20-29	66	349,163	18.9 (14.8-23.9)	5	277,454	1.8 (0.7-4.0)	71	626,617	11.3 (8.9-14.2)
30-39	10	338,255	3.0 (1.5-5.3)	1	288,468	0.3 (0.2-1.7)	11	626,723	1.8 (0.9-3.0)
40-49	4	352,843	1.1 (0.4-2.7)	1	319,724	0.3 (0.1-1.5)	5	672,567	0.7 (0.3-1.6)
10-49	**177**	**1,302,016**	**13.6 (11.7-15.7)**	**15**	**1,138,240**	**1.3 (0.8-2.1)**	**192**	**2,440,256**	**7.9 (6.8-9.0)**
BULIMIA NERVOSA									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence(95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	7	116,476	6.0 (2.6-11.9)	0	120,219	0	7	236,695	2.9 (1.1-5.6)
15-19	68	145,279	46.8 (36.6-58.9)	4	132,375	3.0 (0.9-7.3)	72	277,654	25.9 (20.1-32.4)
20-29	111	349,163	31.8 (26.3-38.1)	13	277,454	4.7 (2.6-7.8)	124	626,617	19.8 (16.4-23.2)
30-39	65	338,255	19.2 (15.0-24.3)	1	288,468	0.3 (0.2-1.7)	66	626,723	10.5 (8.2-13.3)
40-49	18	352,843	5.1 (3.1-7.9)	0	319,724	0	18	672,567	2.7 (1.6-3.8)
10-49	**269**	**1,302,016**	**20.7 (18.3-23.2)**	**18**	**1,138,240**	**1.6 (1.0-2.4)**	**287**	**2,440,256**	**11.8 (10.5-13.2)**
EATING DISORDER NOS (EDNOS)									
Age (years)	Females			Males			Total		
	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)	Cases (N)	Population (N)	Incidence (95% CI)
10-14	39	116,476	33.5 (24.1-45.3)	18	120,219	15.0 (9.1-23.2)	57	236,695	24.1 (18.4-31.0)
15-19	102	145,279	70.2 (57.5-84.9)	14	132,375	10.6 (6.0-17.3)	116	277,654	41.8 (34.7-49.9)
20-29	132	349,163	37.8 (31.8-44.7)	9	277,454	3.2 (1.6-5.9)	142	626,617	22.7 (19.2-26.6)
30-39	63	338,255	18.6 (14.4-23.7)	4	288,468	1.4 (0.4-3.3)	67	626,723	10.7 (8.3-13.5)
40-49	34	352,843	9.6 (6.8-13.3)	2	319,724	0.6 (0.1-2.0)	36	672,567	5.3 (3.8-7.3)
10-49	**370**	**1,302,016**	**28.4 (25.6-31.4)**	**48**	**1,138,240**	**4.2 (3.1-5.5)**	**418**	**2,440,256**	**17.1 (15.5-18.8)**

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Supplemental Table 1: Annual incidence of eating disorders by gender and eating disorder type per 100,000 population

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
All Eating Disorders Incidence (95% CI)	789/2,393,179 33.0 (30.7-35.3)	838/2,673,109 31.4 (29.3-33.5)	953/2,703,550 35.3 (33.1-37.5)	967/2,740,803 35.3 (33.1-37.6)	904/2,827,344 32.0 (29.9-34.1)	906/2,819,275 32.1 (30.0-34.3)	882/2,786,786 31.7 (29.6-33.8)	980/2,680,119 36.6 (34.3-38.9)	946/2,553,593 37.1 (34.7-39.5)	897/2,440,256 36.8 (34.4-39.2)
Females										
All ED Incidence (95% CI)	732/1,374,900 53.2 (49.5-57.2)	777/1,504,681 51.6 (48.0-55.4)	884/1,513,075 58.4 (54.6-62.4)	899/1,518,646 59.2 (55.4-63.2)	839/1,532,386 54.8 (51.1-58.5)	853/1,515,225 56.3 (52.6-60.2)	805/1,486,937 54.1 (50.5-58.0)	894/1,434,592 62.3 (58.3-66.5)	873/1,367,358 63.8 (59.7-68.2)	816/1,302,016 62.7 (58.4-67.1)
AN Incidence (95% CI)	195/1,374,900 14.2 (12.3-16.3)	189/1,504,681 12.6 (10.9-14.5)	177/1,513,075 11.7 (10.1-13.5)	234/1,518,646 15.4 (13.5-17.5)	196/1,532,386 12.8 (11.1-14.7)	188/1,515,225 12.4 (10.7-14.3)	172/1,486,937 11.6 (10.0-13.4)	234/1,434,592 16.3 (14.3-18.5)	196/1,367,358 14.3 (12.4-16.5)	177/1,302,016 13.6 (11.7-15.7)
BN Incidence (95% CI)	294/1,374,900 21.4 (19.0-24.0)	330/1,504,681 21.9 (19.7-24.4)	361/1,513,075 23.9 (21.5-26.4)	378/1,518,646 24.9 (22.5-27.5)	323/1,532,386 21.1 (18.9-23.5)	346/1,515,225 22.8 (20.5-25.3)	312/1,486,937 21.0 (18.8-23.4)	303/1,434,592 21.1 (18.8-23.6)	324/1,367,358 23.7 (21.2-26.4)	269/1,302,016 20.7 (18.3-23.2)
EDNOS Incidence (95% CI)	243/1,374,900 17.7 (15.5-20.0)	258/1,504,681 17.2 (15.1-19.3)	346/1,513,075 22.9 (20.6-25.4)	287/1,518,646 18.9 (16.8-21.2)	320/1,532,386 20.9 (18.7-23.3)	319/1,515,225 21.1 (18.8-23.5)	321/1,486,937 21.6 (19.3-24.0)	357/1,434,592 24.9 (22.4-27.6)	353/1,367,358 25.8 (23.2-28.6)	370/1,302,016 28.4 (25.6-31.4)
Males										
All ED Incidence (95% CI)	57/1,018,279 5.6 (4.3-7.2)	61/1,168,428 5.2 (4.0-6.6)	69/1,190,475 5.8 (4.5-7.3)	68/1,222,157 5.6 (4.3-7.0)	65/1,294,958 5.0 (3.9-6.3)	53/1,304,050 4.1 (3.1-5.3)	77/1,299,849 5.9 (4.7-7.4)	86/1,245,527 6.9 (5.6-8.5)	73/1,186,235 6.1 (4.9-7.7)	81/1,138,240 7.1 (5.7-8.8)
AN Incidence (95% CI)	8/1,018,279 0.8 (0.4-1.5)	12/1,168,428 1.0 (0.6-1.7)	21/1,190,475 1.7 (1.1-2.7)	17/1,222,157 1.5 (0.9-2.3)	4/1,294,958 0.3 (0.1-0.7)	6/1,304,050 0.5 (0.2-0.9)	4/1,299,849 0.3 (0.1-0.7)	18/1,245,527 1.4 (0.9-2.2)	12/1,186,235 1.0 (0.5-1.7)	15/1,138,240 1.3 (0.8-2.1)
BN Incidence (95% CI)	14/1,018,279 1.4 (0.8-2.2)	14/1,168,428 1.2 (0.7-2.0)	14/1,190,475 1.2 (0.7-1.9)	12/1,222,157 1.0 (0.7-1.9)	19/1,294,958 1.5 (0.9-2.3)	15/1,304,050 1.2 (0.7-1.9)	20/1,299,849 1.5 (1.0-2.3)	17/1,245,527 1.4 (0.8-2.1)	21/1,186,235 1.8 (1.1-2.8)	18/1,138,240 1.6 (1.0-2.4)
EDNOS Incidence (95% CI)	35/1,018,279 3.4 (2.4-4.7)	45/1,168,428 3.8 (2.8-5.1)	34/1,190,475 2.9 (2.0-3.9)	39/1,222,157 3.2 (2.3-4.3)	42/1,294,958 3.2 (2.4-4.3)	32/1,304,050 2.4 (1.7-3.4)	53/1,299,849 4.1 (3.1-5.3)	51/1,245,527 4.1 (3.1-5.3)	40/1,186,235 3.4 (2.4-4.5)	48/1,138,240 4.2 (3.1-5.5)

ED: eating disorder; AN: anorexia nervosa, BN: bulimia nervosa, EDNOS: eating disorder not otherwise specified

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

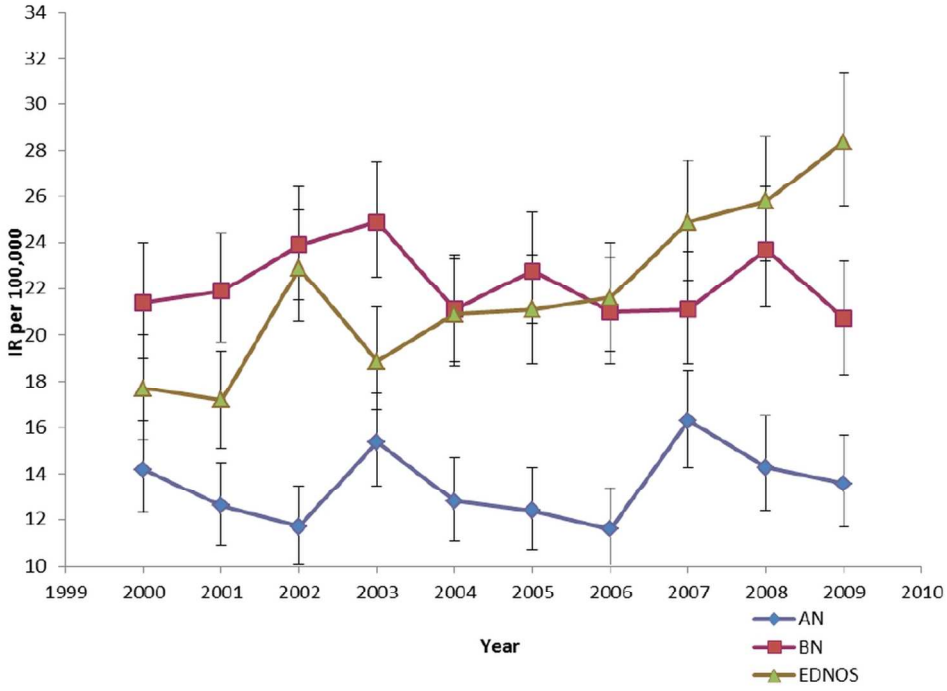
Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	n/a

For Peer Review Only

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

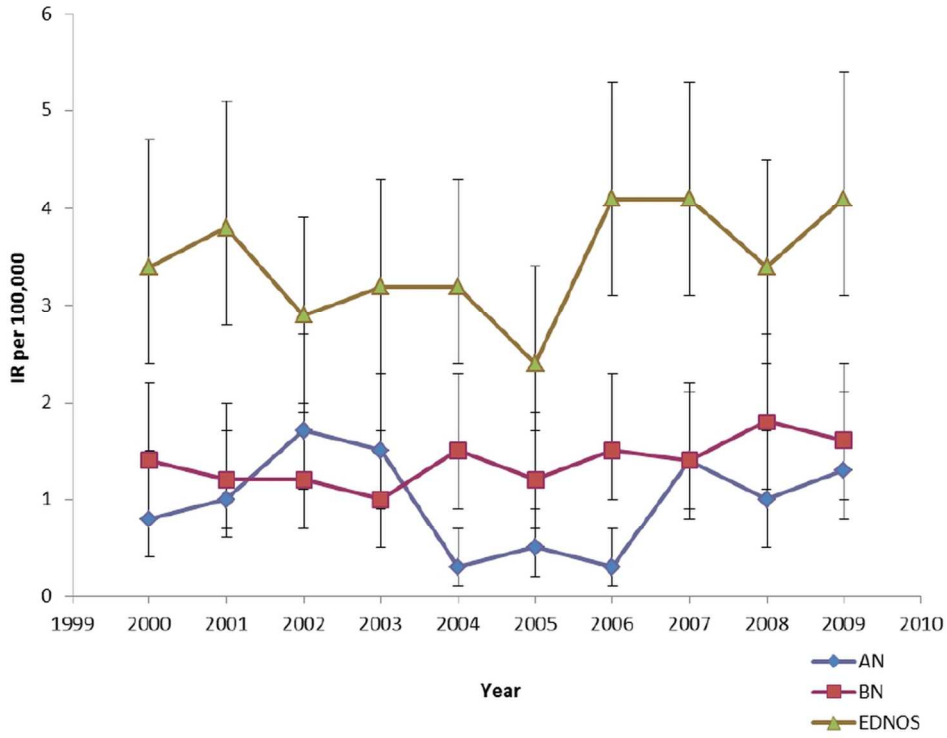
*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only



126x90mm (300 x 300 DPI)

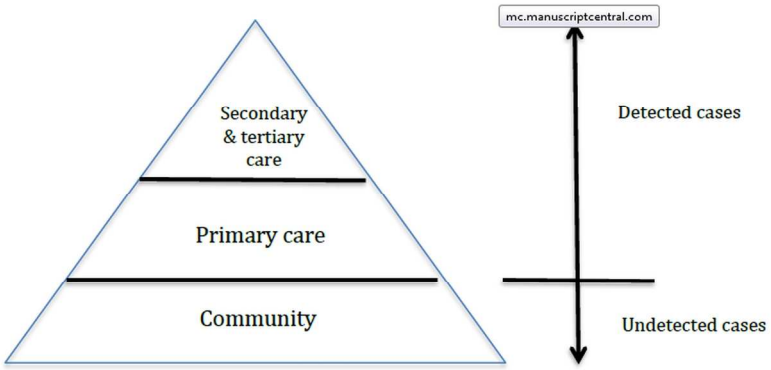
View only



119x90mm (300 x 300 DPI)

For peer review only

Figure 3: Incidence of disorders in the community and in the healthcare setting



205x90mm (300 x 300 DPI)

For peer review only